University of Alberta

ADAPTABILITY OF LOCOMOTION

by

Tania Lam

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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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This thesis is dedicated to my family –

To my father who always encouraged the best from me,
to my stepmother whose support and presence has been a comfort to me,
to my sister for her belief in me and knowing how to make me laugh out loud,
to my Aunt Winny for being there for all of us,
and to the memory of my mother.

Abstract

The control of locomotion must be adaptable to changes to the environment or intrinsic properties of the body in order for an animal to interact meaningfully with its surroundings. Both short-term and long-term adaptive modifications during mammalian locomotion were examined in the projects presented in this thesis. Short-term adaptation of the locomotor pattern to produce different directions of stepping was investigated in human infants, before the onset of independent walking. Most infants could produce treadmill-elicited stepping in different directions and could make a smooth transition between directions of stepping without any discrete changes in muscle activation patterns or the temporal parameters of stepping. The response to changes in treadmill speed was also similar between stepping directions. The results are thus consistent with the idea that central locomotor networks can be adapted to generate different locomotor tasks.

Short-term adaptive responses to changes in muscle afferent feedback during locomotion was investigated in decerebrate cats. Changes in proprioceptive feedback strongly modulated hip flexor activity during the swing phase of treadmill locomotion. Feedback from the sartorius muscles was found to be particularly important in this response. Input from large muscle afferents is likely a major contributor to this modulation since stimulation of the sartorius nerve at stimulus intensities that would preferentially recruit group I muscle afferents produced an increase in hip flexor burst activity during the swing phase of treadmill locomotion. In addition, electrical activation of group II sartorius muscle afferents produced either excitatory or inhibitory effects on flexor burst activity.

How might sustained changes to the neuromuscular or biomechanical properties of the body enable longer-term modifications in the locomotor pattern (learning)? This issue was examined in the final projects, which described the adaptive modifications in response to chronic loading of the limb during the swing phase of locomotion in adult cats and human infants. In adult cats, the main adaptive strategy to loading of the limb was an increase in knee flexor activity during the swing phase. Removal of the load resulted in an after-effect, consistent with the idea that the adaptive modifications involved long-term changes to locomotor generating systems (learning). In human infants, loading of the limb during the swing phase of treadmill elicited stepping resulted in an increase in hip and knee flexor muscle torque during the swing phase. Most infants did not show an after-effect after removal of the weight, suggesting that proprioceptive reflex pathways may have played the primary role in mediating the increase in hip and knee flexor muscle torque during steps taken with the weight on.

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Table of Contents

Chapter 1 - GENERAL INTRODUCTION 1

1.1 Introduction 2

1.2 Central Mechanisms Generating Locomotion 3

1.3 Studying Sub-Cortical Control of Human Locomotion using Infants 7

1.4 Is there Shared Neuronal Circuitry for Different Forms of Locomotion? 12

1.5 The Role of Proprioceptive Feedback in the Regulation and Adaptation of Locomotor Activity 16

- 1.5.1 Afferent Regulation of the Timing of Extensor Burst Activity 16
- 1.5.2 Afferent Regulation of the Magnitude of Extensor Burst Activity 20
- 1.5.3 Segmental Pathways Involved in the Afferent Regulation of Extensor Burst Activity 23
- 1.5.4 Afferent Regulation of the Timing and Magnitude of Flexor Burst Activity 26
- 1.5.5 Segmental Pathways Involved in the Afferent Regulation of Flexor Burst Activity 30

1.6 Adaptive Plasticity in the Walking System 31

- 1.6.1 Adaptive Modifications to Locomotion in Cats after Peripheral Nerve Injury 31
- 1.6.2 Adaptive Modifications to Locomotion after Biomechanical Changes to the Limb 37

1.7 Summary and Thesis Objectives 40

1.8 References 43

Chapter 2 - COULD DIFFERENT DIRECTIONS OF HUMAN INFANT STEPPING BE CONTROLLED BY THE SAME CENTRAL PATTERN GENERATOR? 53

2.1 Introduction 54

2.2 Methods 58

- 2.2.1 Subjects and Preparation 58
- 2.2.2 Data Analysis 60

2.3 Results 63

- 2.3.1 Incidence of Stepping in Different Directions 63
- 2.3.2 Temporal Parameters of Stepping in Different Directions 66
- 2.3.3 EMG Patterns 71
- 2.3.4 Transitions 83

2.4 Discussion 88

2.4.1 Methodological Considerations 88
2.4.2 The Response to Speed is Similar for the Different Directions of Stepping 89
2.4.3 Muscle Activation Patterns in Different Directions of Stepping 90
2.4.4 Backward and Forward Walking are Different between Infants and Adults 92
2.4.5 Conclusions 94
2.5 References 96

Chapter 3 - PROPRIOCEPTIVE MODULATION OF HIP FLEXOR ACTIVITY DURING THE SWING PHASE OF LOCOMOTION IN DECEREBRATE CATS 99

3.1 Introduction 100
3.2 Methods 102
3.2.1 Preparation 102
3.2.2 Data Analysis 107
3.3 Results 108
3.3.1 Sensory Input from Hip Flexor Muscles Influences Flexor Burst Activity 108
3.3.2 Afferents from the Sartorius Muscles are Particularly Important for Flexor Burst Modulation 119
3.3.3 The Influence of Contralateral Limb Activity on Ipsilateral Flexor Burst Activity 125
3.4 Discussion 131
3.4.1 Modulation of Flexor Activity by Flexor Muscle Afferents during the Swing Phase 132
3.4.2 Feedback from the Sartorius Muscles is Important for Enhancing Flexor Burst Activity 138
3.4.3 Functional Relevance 139
3.5 References 140

Chapter 4 - SARTORIUS MUSCLE AFFERENTS INFLUENCE THE AMPLITUDE AND TIMING OF FLEXOR ACTIVITY IN WALKING DECEREBRATE CATS 142

4.1 Introduction 143
4.2 Methods 143
4.2.1 Preparation 145
4.2.2 Data Analysis 147
4.3 Results 147
4.3.1 Effect of Sartorius Group I Afferents on Flexor Burst Duration and Amplitude 147
4.3.2 Effect of Sartorius Group II Afferents on Flexor Burst Duration 153

4.4 Discussion 168
    4.4.1 Action of Sartorius Group I Muscle Afferents 169
    4.4.2 Action of Sartorius Group II Muscle Afferents 173
    4.4.3 Functional Implications and Concluding Remarks 176
4.5 References 177

Chapter 5 - LOADING OF THE LIMB DURING THE SWING PHASE: ADAPTIVE STRATEGIES FOR STEPPING OVER OBSTACLES 179

5.1 Introduction 180
5.2 Methods 182
    5.2.1 Preparation and Training 182
    5.2.2 Data Analysis 185
5.3 Results 190
    5.3.1 Obstacle Avoidance with Loading of the Limb – Trailing over the Obstacle 191
        5.3.1a Cat 1 – Kinematics and EMG Patterns 191
        5.3.1b Cat 2 – Kinematics and EMG Patterns 196
    5.3.2 Leading Steps vs. Trailing Steps over the Obstacle – Kinematics and EMG Patterns 201
    5.3.3 Obstacle Avoidance with Loading of the Limb and PbST Denervation 202
        5.3.3a Incidence of Errors 205
        5.3.3b Leading Steps over the Obstacle – Kinematics, EMG Patterns, and Joint Torques 208
        5.3.3c Trailing Steps over the Obstacle – Kinematics, EMG Patterns, and Joint Torques 218
5.4 Discussion 227
    5.4.1 Methodological Considerations 228
    5.4.2 Knee Flexor Activity Plays an Integral Role in the Adaptive Response to Additional Loading of the Limb during Obstacle Avoidance 230
    5.4.3 Implications of After-Effects – Was There Learning? 233
    5.4.4 Conclusions 237
5.5 References 238

Chapter 6 - HOW DO INFANTS ADAPT TO LOADING OF THE LIMB DURING THE SWING PHASE OF STEPPING? 242

6.1 Introduction 243
6.2 Methods 244
    6.2.1 Subjects and Preparation 244
    6.2.2 Data Analysis 246

6.3 Results 248
6.3.1 Kinematics 252
6.3.2 Hip Torques 259
6.3.3 Knee Torques 265
6.3.4 Quantification of Muscle Torques 268
6.4 Discussion 271
6.5 References 276

Chapter 7 - GENERAL DISCUSSION 278

7.1 Summary 279
7.2 Future Directions 280
7.2.1 Neural Control of Different Forms of Locomotion 280
7.2.2 Proprioceptive Regulation of Flexor Activity during the Swing Phase of Walking 283
7.2.3 Learning during Walking Tasks 285
7.3 References 291

Appendix 1 - EQUATIONS OF MOTION FOR THE ESTIMATION OF JOINT TORQUES DURING THE SWING PHASE OF LOCOMOTION 293

References 297

List of Tables

Table 2.1. Number of Infants who Contributed EMG Data 80

Table 4.1. Effects of 3-5 *T* Sartorius Nerve Stimulation. 161

Table 5.1. Comparison of Swing Phase Velocity (m/s) between Cats and between Stepping Conditions 189

List of Figures

Figure 1.1. Muscle Afferent Pathways Regulating Extensor and Flexor Activity during Locomotion. 25

Figure 1.2. Adaptive Modifications of the Locomotor Pattern following Partial Denervation of Ankle Extensors. 35

Figure 2.1. Incidence of Backward and Sideways Stepping. 65

Figure 2.2. Kinematic Figure of Forward, Backward, and Sideways Stepping. 68

Figure 2.3. The Response to Changes in Treadmill Speed. 70

Figure 2.4. Phase Duration vs. Cycle Duration. 73

Figure 2.5. Index of Co-Contraction during Forward, Backward, and Sideways Stepping. 75

Figure 2.6. Muscle Activation Patterns for Different Directions of Stepping. 77

Figure 2.7. EMG Patterns Averaged across Subjects for Different Stepping Directions. 82

Figure 2.8. Transitions between Different Directions: Temporal Patterns during Stepping. 85

Figure 2.9. Transitions between Different Directions: Muscle Activation Patterns during Stepping. 87

Figure 3.1. Illustrations of the Experimental Preparation used to Apply Perturbations during the Swing Phase. 106

Figure 3.2. Effect of Manual Assistance during Swing. 110

Figure 3.3. Effect of Manual Resistance during Swing. 113

Figure 3.4. Group Data for the Response to Manual Perturbations. 115

Figure 3.5. Effect of Blocking Hip Flexion during Swing. 118

Figure 3.6. Effect of IP Tenotomy on the Response to Blocking Hip Flexion. 121

Figure 3.7. Response to IP Stretch during Walking. 124

Figure 3.8. Effect of Blocking Conduction in the Sartorius Nerves on the Response to Blocking Hip Flexion. 127

Figure 3.9. The Effect of Delaying the Onset of Contralateral Flexor Activity. 130

Figure 3.10. Schematic Diagram of Hypothesized Afferent Pathways from Flexor Muscles that Enhance Flexor Activity. 134

Figure 4.1. The Effect of 1.6 *T* Sartorius Nerve Stimulation during the Flexor Phase of Locomotion. 149

Figure 4.2. The Effect of Sartorius Nerve Stimulation at Group I Strengths on IP and TA Burst Activity. 152

Figure 4.3. The Effect of Sartorius Nerve Stimulation at 1.6 and 1.8 *T* on Locomotor Cycle Period. 155

Figure 4.4. The Effect of Activating Group II Sartorius Muscle Afferents during the Flexor Phase of Locomotion 157

Figure 4.5. The Effect of 5 *T* Sartorius Nerve Stimulation on Flexor Burst Activity during Locomotion. 163

Figure 4.6. Stimulating the Sartorius Nerve at Group II Strengths Produced Varying Results. 166

Figure 4.7. Schematic Diagram of Sartorius Muscle Afferent Feedback Pathways Involved in the Modulation of Flexor Activity during Locomotion. 172

Figure 5.1. Cat 1 – Kinematic Patterns from Trailing Steps over the Obstacle 193

Figure 5.2.Cat 1 – EMG Patterns from Trailing Steps over the Obstacle. 195

Figure 5.3. Cat 2 – Kinematic Patterns from Trailing Steps over the Obstacle 198

Figure 5.4. Cat 2 – EMG Patterns from Trailing Steps over the Obstacle. 200

Figure 5.5. Comparison of Kinematic and EMG Patterns during Leading and Trailing Steps over the Obstacle 204

Figure 5.6. Number of Errors after Addition of the Weight and PbST Neurectomy during Obstacle Avoidance 207

Figure 5.7. Kinematic Patterns from Leading Steps over the Obstacle after PbST Neurectomy. 210

Figure 5.8. Muscle Activation Patterns from Leading Steps over the Obstacle after PbST Neurectomy. 214

Figure 5.9. Joint Torques during Leading Steps over the Obstacle after PbST Neurectomy. 216

Figure 5.10. Kinematic Patterns from Trailing Steps over the Obstacle after PbST Neurectomy. 220

Figure 5.11. Muscle Activation Patterns from Trailing Steps over the Obstacle after PbST Neurectomy. 223

Figure 5.12. Joint Torques during Trailing Steps over the Obstacle after PbST Neurectomy. 226

Figure 6.1. Grouping of Infants - After-Effects and No After-Effects....................251

Figure 6.2. Changes in Toe Trajectory with the Weight On and Off. 254

Figure 6.3. Repeated Trials with the Weight On. 257

Figure 6.4. Change in Kinematic Variables with the Weight On and Off. 261

Figure 6.5. Averaged Hip Torques with the Weight On and Off....................263

Figure 6.6. Averaged Knee Torques with the Weight On and Off. 267

Figure 6.7. Quantification of Hip and Knee Muscle Torques. 270

List of Abbreviations

lateral gastrocnemius/soleus	LGS
iliopsoas	IP
tibialis anterior	TA
extensor digitorum longus	EDL
posterior biceps and semitendinosus	PbST
medial gastrocnemius	MG
gastrocnemius/soleus	GS
quadriceps	Quad
hamstrings	Hams
anterior head of sartorius	SartA
medial head of sartorius	SartM
rectus femoris	RF
flexor digitorum longus	FDL
central pattern generator	CPG
electromyographic/electromyography/electromyogram	EMG
cord dorsum potential	CDP

CHAPTER 1

GENERAL INTRODUCTION

Some sections were adapted from an original publication:
T. Lam and K. G. Pearson
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1.1 Introduction

The motor system supplies the basic tools for the survival of all animals, vertebrates and invertebrates alike. Without movement, the ability to perform such basic activities as feeding and breathing would be impossible. The ability to move within the surrounding environment would also be greatly compromised and limit the ability to forage or hunt for food, defend against predators, and seek safe shelter. Even the communication of our thoughts and ideas would be unavailable were it not for the motor system.

Among the species of the animal kingdom, the ability to locomote, or move actively in space, is a common characteristic. Whether it is crawling, swimming, flying, or walking, all vertebrates have the ability to manipulate their bodies around the environment. As with many processes of the nervous system, the fundamental principle underlying the production of locomotion is rhythmicity. The control of this locomotor rhythmicity is one of the most studied areas in motor control neuroscience. To date, the intricacies of the neuronal circuitry involved in the central generation of mammalian locomotion remain unknown. On the other hand, it is obvious that locomotion is highly flexible and malleable to new environments, changes in sensory input, and changes to the properties of the body. This thesis addresses 3 issues related to the adaptability of the mammalian locomotor rhythm: short-term adaptation of the locomotor circuitry to produce different forms of walking, short-term adaptation to phasic changes in sensory input, and longer-term adaptive modifications of the locomotor pattern in response to more sustained changes in sensory input (learning). In this introductory section, a general overview of the background and major concepts related to these areas will be provided. Although it is recognized that shaping and adaptation of locomotor output can originate from a variety of sources (e.g. cutaneous feedback, input from supraspinal nervous centres), the discussion will be limited to those issues pertaining to the data presented in this thesis.

1.2 Central Mechanisms Generating Locomotion

The spinal origin of such fundamental behaviours as stepping, standing, or scratching has been recognized for some time (Sherrington 1906, 1910a, b). Early ideas on the spinal control of locomotion fell into two distinct groups. One argument expounded the idea that locomotion could be produced solely by a feedback system of peripheral reflexes (Sherrington 1910a). The alternative idea was that centres within the nervous system control the activation and coordination of muscles involved in locomotion without relying on peripheral reflexes. Direct support for this second hypothesis was supplied early on by Brown (1911) who showed that alternating flexion and extension activity could still be generated in spinal decerebrate cats despite transection of all the dorsal roots. He proposed the existence of paired flexor and extensor half-centres ('intrinsic factors') in the spinal cord with mutual inhibitory connections that are responsible for generating the basic locomotor rhythm. While demonstrating that central mechanisms determine the basic stepping pattern, Brown did not discount the role of peripheral stimuli in shaping the output generated by these central mechanisms ("*. . . the part which they play is essentially the regulative – not the causative*") (Brown 1911). These original ideas, formulated almost a century ago, have provided the guiding principles in the study of the neural control of locomotion today.

In the 1960s, Jankowska et al. (1967a) showed that electrical stimulation of non-nociceptive high-threshold muscle, joint, and cutaneous afferents ('flexor reflex afferents', or FRA) produced long-lasting excitation of ipsilateral flexor motoneurons and inhibition of extensor motoneurons in acute spinal cats after administration of the noradrenergic agonist, L-dihydroxyphenylalanine. Electrical stimulation of the contralateral FRA produced the opposite effect (excitatory response of ipsilateral extensors and inhibitory response of contralateral flexors). In addition, Jankowska et al. (1967a, b) reported that stimulation of the FRA could sometimes produce a series of alternating flexor and extensor bursts similar to locomotor activity. Evidence for mutual inhibition between the extensor and flexor centres was supplied by the fact that an excitatory response was suppressed by a conditioning stimulus to the antagonistic group of interneurons. Taken together, these observations led to the proposal that the neuronal network producing these alternating flexor and extensor bursts might be related to the generation of locomotion (Jankowska et al. 1967a, b) and corroborated the hypothesis of Brown (1911) that flexor and extensor half-centres within the spinal cord mutually inhibit each other and form the basic circuitry for generating locomotion.

A problem with Brown's half-centre model for locomotion is that it cannot account for all aspects of the typical locomotor activity pattern. The half-centre hypothesis allows for only a simple alternation between flexors and extensors during walking. While extensor activity during stepping is mainly uniform (single-joint extensor muscles active throughout the stance phase), flexor activity can be distinct among individual flexor and bifunctional muscles (Engberg and Lundberg 1969). Engberg and Lundberg (1969) thus proposed that aspects of flexor burst activity (such as the late-swing burst in the semitendinosus muscle) are modulated by afferent input. Grillner and Zangger (1975, 1979, 1984) later challenged this idea by showing that muscle activation patterns during treadmill locomotion in spinal and decerebrate cats does not revert to a simple flexion-extension alternation after transection of lumbar dorsal roots. While the central origin of the locomotor pattern was not disputed, the degree to which peripheral input is required in order to produce the basic locomotor pattern of an intact animal was a point of contention (Grillner 1981; Lundberg 1981).

As a result of these findings, alternative, or adjunct, models to the half-centre hypothesis have been proposed. Grillner proposed an alternative to the half-centre model of locomotion, which he termed the locomotor 'central pattern generator' model (Grillner 1981). The main premise of this model is that the network controlling locomotion is subdivided into networks controlling different limbs which in turn may be further subdivided into networks that control individual muscle groups ('unit burst generators'). This organizational model has been used to account for the motor patterns of the turtle scratch reflex and modified to account for motor patterns during the cat scratch reflex, paw-shake response, and different forms of cat locomotion (Stein and Smith 1997). Alternatively, Perret and Cabelguen (1980) proposed that some motoneurons, specifically those innervating bifunctional muscles, receive commands from both the flexor and extensor half-center (see also Orsal et al. 1986). Grading the relative strengths of the inputs from the two half-centres would thus determine the phasing of the muscle's activity. Input to bifunctional motoneurons would originate primarily from one of the half-centres (e.g. for semitendinosus, the main input would originate from the extensor half-centre) and input from the other half-centre would arrive via a set of intervening interneurons (Perret 1983;

Orsal et al. 1986). Both Grillner's and Perret's model promote the idea that some of the basic characteristics of the locomotor pattern (such as the double burst of activity in semitendinosus or rectus femoris muscles) can be generated within central networks. These models also offer the attractive possibility that similar motor tasks (e.g. scratching and locomotion, or forward and backward walking) may share components of a common pattern generating network (Grillner 1981; reviewed in Stein and Smith 1997).[1]

Is there a locomotor central pattern generator (CPG) in humans like that described in animal preparations (Brown 1911; Grillner 1981)? Unlike results from animal studies that showed that locomotor patterns could be recorded despite spinalization and deafferentation, there is no direct evidence for the existence of a CPG for locomotion in humans. There are some reports that individuals with incomplete or complete spinal cord injury can generate stepping-like movements, which lends support for the existence of spinal locomotor networks in humans (Calancie et al. 1994; Dietz et al. 1995; Dimitrijevic et al. 1998). In addition, indirect evidence based on reflex responses in complete spinal cord injured individuals also indicates the presence of spinal reflex circuitry whose design would be consistent with a spinal rhythm generator for locomotion in humans (Roby-Brami and Bussel 1987; Bussel et al. 1988, 1989). However, full convincing evidence for the existence of a locomotor CPG in humans could only be obtained in the unlikely situation of an individual with a complete spinal cord injury and *complete* deafferentation of the lower limbs (i.e. analogous to fictive spinal animal preparations) who could be made to produce stepping movements. Investigators who have attempted to address this issue in primate preparations have yielded inconclusive results (Eidelberg et al. 1981; Fedirchuk et al. 1998). Eidelberg et al. (1981) were unable to elicit any stepping in acutely spinalized macaques despite application of pharmacological agents after recovery from spinal shock. Fedirchuk et al. (1998) also reported that only components of the fictive locomotor pattern could be obtained after administration of monoaminergic agents or excitatory amino acids to acutely spinalized marmoset monkeys. Whether or not these "components" of the fictive locomotor pattern actually represent a part of the output of the putative spinal locomotor generator remains to be investigated in further detail.

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[1] The term 'central pattern generator' is used throughout this thesis to refer to the spinal interneuronal network that generates the basic locomotor pattern and does not necessarily refer specifically to Grillner's (1981) model.

1.3 Studying Sub-Cortical Control of Human Locomotion using Infants

Much of our understanding of the neural control of mammalian locomotion stems from results obtained from animal preparations. For example, detailed knowledge of the influence of sensory feedback from muscle receptors on the timing of the locomotor pattern at the spinal level has accumulated from reduced cat preparations (reviewed in Pearson 1995; McCrea 2001). Whether sensory feedback is processed in the same way to regulate the timing of the locomotor pattern during human walking is unclear (Stephens and Yang 1999). However, results from uninjured adult humans are likely confounded by influences from postural control and volitional responses (Misiaszek et al. 2000). Differences between results obtained from uninjured adult humans and those obtained from other vertebrate preparations may also reflect a fundamental difference in the control of locomotion between species. Indeed, conclusive evidence for the very existence of a locomotor spinal pattern generator in humans remains to be obtained. Assuming that there is a locomotor spinal pattern generator in humans, experiments to examine the characteristics of this circuitry would be difficult in human subjects. First, spontaneous recovery of stepping is rare in subjects with spinal cord injuries (Calancie et al. 1994) and often requires months of intensive treadmill training or other types of interventions to produce regular patterns of rhythmic stepping (Wernig and Müller 1992; Dietz et al. 1995; Dimitrijevic et al. 1998). Second, plastic changes within the spinal cord associated with therapy or training and to the injury itself inevitably occur and how these changes would alter any original locomotor-related circuitry in the spinal cord is not clear. How might we then approach the control of human locomotion at the spinal cord level without the intervention of factors such as volitional control or injury-induced plasticity? To address this issue, recent investigations have focused on the neural control of stepping in human infants less than 12 months old (before the onset of independent walking) (Yang et al. 1998a, b; Lamb and Yang 2000; Pang and Yang 2000, 2001).

Even in utero (DeVries et al. 1984) and early after birth (McGraw 1940; Peiper 1963), human infants show a stepping response. Anencephalic infants also have this response, thus showing the capacity for brainstem and/or spinal structures for controlling this stepping response (Peiper 1963). In healthy infants, the stepping response is present throughout the first year of life, except for a period starting at 2 months of age and lasting until 6 to 8 months of age during which the stepping response is usually difficult to elicit (McGraw 1940). However, daily practice of stepping has been shown to minimize the difficulty in eliciting this response during this period (Zelazo et al. 1972; Yang et al. 1998a). The stepping response is usually elicited by holding the infant upright either over a moving treadmill or by slowly moving the body forward over a stationary surface (McGraw 1940; Peiper 1963; Forssberg 1985; Yang et al. 1998a). Although many specific characteristics of the adult walking pattern are missing in the infant stepping response, Forssberg (1985) has suggested that the same neural networks that produce the early stepping response in young infants is also involved in the production of walking in adults. For example, infants and young children display a digitigrade pattern of stepping where contact is made with the forefoot and there is no heel strike. With the onset of independent, non-supported walking early in the first year of life, this digitigrade pattern of stepping continues. Thus, although the children have developed the ability to voluntarily control their locomotor activity, an infantile pattern of walking persists. The gradual emergence to a plantigrade pattern of gait occurs later in the 2nd year of life, well after the development of independent walking (Forssberg 1985).

An important assumption of infant stepping studies is that descending cortical input is sufficiently immature to provide any significant influences on stepping mechanisms in brainstem or spinal structures. This assumption is based on histological, electrophysiological, imaging, and behavioural observations (as described in the preceding paragraph) in human infants. Histological and imaging studies have shown that while many of the descending pathways from the brainstem are well myelinated by birth (reviewed in Sarnat 1989; Hashimoto et al. 1994; Dambska and Kuchna 1996), development of descending input from the cerebellum and the cortex continues throughout the first year of life and beyond (Yakovlev and Lecours 1967; Rorke and Riggs 1969; Brody et al. 1987).

Many of the descending pathways originating from the brainstem are well myelinated and functioning by birth in humans (Sarnat 1989). The perinatal period is perhaps the time during which these pathways play their most important role in reflexive functions in infants. Moreover, morphometric studies have shown that the brainstem undergoes the greatest maturation during fetal life in order to develop to the level required for independent life in the newborn (Dambska and Kuchna 1996). Thus, by birth, we assume that descending brainstem pathways could be functioning to activate possible locomotor centres in the infant spinal cord.

Development of the cerebellum is also progressing by birth. Phylogenetically older areas of the cerebellum are functional by 5 weeks of age, as shown by glucose metabolism during PET scan (Chugani and Phelps 1986) and anatomical studies (Yakovlev and Lecours 1967). By 3 months of age, glucose metabolism shown by PET scanning extends to the cerebellar hemispheres (Chugani and Phelps 1986) and spinocerebellar fibres are near fully myelinated (Yakovlev and Lecours 1967). However, myelination and activity of the cerebellum during the first year of life does not necessarily correspond with mature function. For example, the development of coordinated movements associated with cerebellar function is protracted throughout childhood (Connolly and Forssberg 1997). While reflexes involving primitive cerebellar pathways, such as optical, labyrinthine, and body-righting reflexes, are developed within 6 months after birth, other behaviours influenced by the cerebellum are not refined until later. The ability of an infant to make a smooth and accurate arm movement towards a target develops by around 9 months of age and refinements to interlimb coordination during such activities as walking, running, or skipping continues to be refined throughout childhood (Connolly and Forssberg 1997). Thus, it may be concluded that the cerebellum does not acquire its ability to refine movement until at least near the end of the first post-natal year in human infants.

Development of function in descending input from the motor cortex is even more protracted. Although the corticospinal tract reaches the lumbosacral spinal cord by term

(Humphrey 1960), myelination is far from complete at this time (Yakovlev and Lecours 1967; Brody et al. 1987). According to magnetic resonance imaging studies, key connections in the brain that project to the spinal cord, such as the corticospinal pathway at the level of the internal capsule, do not begin myelination until 9 months post-natally (Holland et al. 1986) and are not completely myelinated until the end of the eleventh month post-partum (Barkovich et al. 1988). Some authors have estimated that full myelination of the corticospinal tract is not complete until the age of 2 (Yakovlev and Lecours 1967).

Clinically, some reflex responses of infants often resemble those of adults with corticospinal tract lesions. For example, the Babinski response is extensor in infants as it is in adults with corticospinal lesions (Connolly and Forssberg 1997). In addition, H-reflexes can be elicited in the small muscles in the hand and foot in infants, a response that is not present in humans over 2 years old but can be recorded in adults with cortical lesions (reviewed by Mayer and Mosser 1973; Vecchierini-Blineau and Guiheneuc 1981). Infants also demonstrate 'reflex irradiation', consisting of short-latency excitation from neighbouring as well as antagonist muscles, in response to simple tendon taps (Myklebust and Gottlieb 1993). This is thought to be due to an increase in the excitability of neurons in the spinal cord secondary to an immature system of descending tracts from the brain (Mayer and Mosser 1973; Vecchierini-Blineau and Guiheneuc 1981; Myklebust et al. 1986; Myklebust and Gottlieb 1993; Leonard et al. 1995). In addition, differences in cutaneous reflex responses are also consistent with the immaturity of function of descending input in infants. In children, the appearance of the long-latency reflex component in response to cutaneous nerve stimulation is not observed until about 15 to 18 months of age (Issler and

Stephens 1983; Rowlandson and Stephens 1985). This component of the cutaneous reflex response is likely mediated by supraspinal pathways (Choa and Stephens 1982; Jenner and Stephens 1982; Evans et al. 1989; Gibbs et al. 1995). The maturation of the corticospinal pathway has also been assessed from electrophysiological recordings from young infants (Koh and Eyre 1988). In children under the age of 1, the threshold for eliciting activity in upper and lower limb muscles in response to transcranial magnetic stimulation over the motor cortex is very high; often, responses are difficult to record without background muscle activity (Koh and Eyre 1988; Eyre et al. 1991; Müller et al. 1991). In addition, conduction velocities within the descending motor tracts are very slow in young infants and do not actually reach adult values in children until 11 years of age (Koh and Eyre 1988). Thus, observations from a variety of experimental approaches lend support to the assumption that much of the behaviour observed in infants younger than 12 months old are mediated by sub-cortical pathways. Based on this, it is reasonable to suggest that infant stepping is mainly mediated by sub-cortical structures and subject to less cortical influence than in adults.

1.4 Is there Shared Neuronal Circuitry for Different Forms of Locomotion?

One of the implications of the central pattern generator model proposed by Grillner (1981) or of the half-centre model including premotor interneuronal networks proposed by Perret (1983) is that the output of the network can vary depending on the pattern of activation and modulation within the neuronal circuit. Indeed, many motor tasks involve similar patterns of activation of muscle groups, for example, the basic alternating pattern of flexor and extensor muscle groups in the lower limbs is used in walking, swimming, and cycling. With regards to the organization of the premotor interneuronal circuitry, one might imagine that individual motor tasks are associated with a particular set of interneurons or that the same premotor circuitry is used for a given set of motor tasks but that different modulatory mechanisms are applied to produce a variety of motor outputs. Across the animal kingdom, there exist numerous examples that uphold the concept of sharing and interaction among interneuronal networks controlling different motor behaviours (reviewed in Dickinson 1995; Marder and Calabrese 1996; Selverston et al. 1997). One of the most compelling sets of data supporting this concept comes from studies of the crustacean stomatogastric nervous system. Numerous modulatory inputs (neuropeptides, amines, and amino acids) to the stomatogastric ganglion have been identified. In addition, neurons in the stomatogastric ganglion possess different combinations of receptors to these modulatory substances (reviewed in Marder and Bucher 2001). Manipulation of the modulatory environment enables control of the frequency and phasing of the units within the stomatogastric circuit to produce the desired motor output, based on the relative sensitivity of the neurons to the different neuromodulators and the ensuing effect on intrinsic membrane properties and synaptic strength.

There is also evidence from simple vertebrate preparations for sharing of circuitry for different motor behaviours. Within the CPG for swallowing, for example, there is evidence that some neurons also contribute to the production of respiration, mastication, or vocalization (reviewed in Jean 2001). Lieske et al. (2000) have shown that in *in vitro* brainstem slice preparations from mice, different respiratory patterns, analogous to sighing, gasping, and regular breathing, are primarily controlled by neurons located in the same region of the slice (and which correspond to the ventral respiratory group, or pre-Bötzinger complex). Furthermore, intracellular recordings from neurons in this region showed that the same neurons received synaptic input during both regular breathing and sighing, or regular breathing and gasping, thus indicating that the three breathing patterns are produced by reconfigurations of the same neuronal network (Lieske et al. 2000).

Sharing of neuronal networks governing different swimming behaviours has also been shown. For example, intracellular recordings from the spinal cord of *xenopus* embryos show that the majority (about 75%) of motoneurons and interneurons that are involved in swimming also fire during struggling (Soffe 1993). Additional interneurons, not active during swimming yet of the same type as those recruited during swimming, were recruited during the struggling behaviour. This additional recruitment of interneurons demonstrated a correlate of the switch from swimming to struggling (Soffe 1993). In the lamprey swimming system, switching from one swimming behaviour to another can result from adjusting the gradient of excitation along the nerve cord. Manipulating the modulatory environment so that caudal segments receive more excitatory input than rostral segments results in a fictive swimming pattern than resembles backward swimming (Matsushima and Grillner 1992).

Similar sharing of circuitry controlling different forms of the scratch reflex in turtles is also thought to exist (reviewed in Stein and Smith 1997; Stein et al. 1998). The turtle scratch reflex has three basic forms and there is strong evidence to suggest that these three forms share the same neural circuitry (Stein et al. 1998). In addition, certain forms of the turtle scratch reflex share similarities with aspects of the movement pattern found in forward stepping, forward swimming, or backpaddling in turtles (Earhart and Stein 2000b). By comparing the pattern of muscle activity, relative phasing of knee movement, and relative durations of hip extension and flexion, Earhart and Stein (2000b) were able to define a range in the parameters of movement during these behaviours. Presumably, different combinations of activation patterns within a shared circuitry could account for the appearance of these different behaviours (Earhart and Stein 2000b). Similarly, parallels in the movement kinematics of hatching, walking, and swimming behaviours in chicks led Bekoff (1992) to suggest that the same motor pattern generator may be reconfigured to produce these different behaviours. Sharing of circuitry controlling different forms of locomotion is also indicated by behavioural studies comparing different directions of locomotion, crouched walking, and slope walking (Buford and Smith 1990; Smith et al. 1993; Trank et al. 1996; Carlson-Kuhta et al. 1998; Smith et al. 1998).

Interaction among neuronal networks controlling rhythmic behaviours is also demonstrated by studies that show coordination between different motor tasks. For example, coordination between swallowing and respiration was recognized early on to be important in order to prevent aspiration (Miller and Sherrington 1916, reviewed in Dickinson 1995). In the lower limb, Earhart and Stein (2000a) showed that the rostral scratch reflex and forward swim stroke of spinal turtles could be blended into a single behaviour that incorporates the motor pattern of each individual task (the 'scratch-swim hybrid'). Similar coordination of two behaviours has also been shown for paw-shaking and locomotion in intact and spinal cats (Carter and Smith 1986a, b). When the paw-shake response was induced during the swing phase of walking, automatic adjustments in the timing of swing and stance durations of all the limbs to preserve interlimb coordination occurred. Furthermore, there were smooth transitions between the muscle synergies used for paw-shaking and those used for swing phase and initial stance phase activity (Carter and

Smith 1986a). The fact that similar adjustments could be made in chronic spinal cats suggests that the mechanisms for rapidly switching from the walking synergy to the paw-shake synergy resides in the spinal cord and is consistent with either a common neural network mediating these two behaviours and/or coupling and sharing of certain components of circuitries that mediate walking and paw-shaking (Carter and Smith 1986b).

In humans, demonstration of smooth switches between different directions of stepping (Lamb and Yang 2000 (see Chapter 2)) and from walking to running (Nilsson et al. 1985; Thorstensson and Roberthson 1987), provide behavioural evidence consistent with the concept of a common locomotor control system for different locomotor tasks. Additionally, Earhart et al. (2001) recently showed that the after-rotation effects following forward walking on a rotating disk were similar between forward and backward walking. They concluded that adaptations of the locomotor system to walking forwards on a rotating disk also transferred to backwards walking, lending further support for the idea that forward and backward walking share locomotor control mechanisms. Similar adaptation can also transfer between stepping and hopping, but to a lesser extent (Earhart et al. 2002). Thus, results from both adult and infant humans show the capability of locomotor control centres to produce variations on the basic locomotor pattern, depending on the requirements of the task.

1.5 The Role of Proprioceptive Feedback in the Regulation and Adaptation of Locomotor Activity

1.5.1 Afferent Regulation of the Timing of Extensor Burst Activity

Shaping of the basic locomotor pattern by sensory input is essential for meaningful locomotion to take place in changing conditions. Early in the last century, Sherrington

(1910a) recognized the crucial role of sensory input in triggering and regulating locomotion. These original ideas were not further explored until almost 70 years later. Much of the recent work on the proprioceptive regulation of stepping has been directed at extending ideas drawn from initial studies by Duysens and Pearson (1980) and Grillner and Rossignol (1978) on afferent mechanisms regulating stance phase duration. Duysens and Pearson (1980) proposed that unloading of the support limb promotes the transition from stance to swing whereas Grillner and Rossignol (1978) proposed that extension of the hip joint is an important factor in promoting this transition. It is now quite apparent that both load- and length-related sensory inputs are involved (reviewed in Pearson 1995; Rossignol 1996; Zehr and Stein 1999; Duysens et al. 2000).

Numerous observations have demonstrated that load-sensitive afferents influence the timing of the locomotor rhythm in cats (Duysens and Pearson 1980; Conway et al. 1987; Pearson et al. 1992; Pearson and Collins 1993; Whelan et al. 1995a). The most direct evidence is that rhythmic force pulses delivered to ankle extensor muscles via electrical stimulation of the L7 ventral roots entrains the locomotor rhythm in acute spinal cats (Pearson et al. 1992). Entrainment of the locomotor rhythm in spinal cats can also be achieved by applying large amplitude stretches to the ankle extensor muscles but not by the application of low amplitude muscle stretches or vibrations, which would preferentially only activate muscle spindles (Conway et al. 1987; Pearson et al. 1992; Pearson and Collins 1993). In addition, electrical stimulation of group I afferents from the ankle extensor muscles, particularly from the lateral gastrocnemius/soleus (LGS), increases stance phase duration and cycle period in decerebrate walking cats (Whelan et al. 1995a). All these observations indicate that force-sensitive Golgi tendon organs strongly influence the locomotor rhythm generating network.

An important role for length-sensitive muscle spindle afferents in the timing of locomotor activity was first suggested by the observation that sinusoidal hip movements could entrain the locomotor rhythm in the hindlimb of spinal (Andersson and Grillner 1983) and decerebrate cats (Kriellaars et al. 1994). Denervation of afferents from the hip joint capsule did not affect the entrainment while progressive elimination of afferent input from various hip muscles led to a weakening of the entrainment (Kriellaars et al. 1994). These findings, along with the fact that Golgi tendon organ responses are weakened in paralyzed preparations (Prochazka and Wand 1980), led to the conclusion that the entrainment by sinusoidal hip movements was largely dependent on spindle afferents arising from different muscles around the hip.

Subsequent experiments by Hiebert et al. (1996) provided direct evidence that spindle afferents from hip muscles influence the timing of the locomotor rhythm. They found that activation of Ia afferents from the hip flexor muscle iliopsoas (IP) by ramp stretches or vibration promoted an earlier onset of flexor activity in walking decerebrate cats and could also entrain the locomotor rhythm. Activation of spindle afferents from ankle flexor and extensor muscles also influences the timing of the locomotor rhythm (Guertin et al. 1995; Hiebert et al. 1996). The fact that ankle extensor group Ia afferents can influence the locomotor rhythm in decerebrate cats (Guertin et al. 1995) but not in spinal cats (see above, Conway et al. 1987; Pearson et al. 1992) may reflect a difference between the decerebrate and spinal cat preparations. Secondary muscle spindles from flexor muscles are also effective in influencing the locomotor rhythm since activation of group II muscle afferents from the tibialis anterior (TA) during extension promoted flexor activity in decerebrate walking cats (Hiebert et al. 1996). On the other hand, in fictive decerebrate cats, stimulation of group II afferents from the sartorius muscle during extension prolonged the extensor phase (Perreault et al. 1995). Notwithstanding the latter observation, the main functional implication of recent findings on the role of muscle spindles in flexor muscles is that lengthening of the flexor muscles at the end of stance facilitates the termination of extensor activity, thus contributing to the triggering of the stance-to-swing transition.

The question of whether afferent feedback is important for regulating the timing of extensor activity during human walking has also been examined (Stephens and Yang 1999, Stein et al. 2000, reviewed in Duysens et al. 2000). Stephens and Yang (1999) reported a small effect on stance and cycle duration with the application of an additional 30% of body weight load to the legs. Similarly, Misiaszek et al. (2000) observed slight changes in the timing of the stance to swing transition when load was applied along the long axis of the leg during supported walking (by holding a rail) in adult humans. The absence of marked effects on timing may be due to the fact that subjects were forced to walk at a constant rate on a treadmill. When the subjects did not support themselves, a prolongation of stance duration was seen in the experiments of Misiaszek et al. (2000), but this was accompanied by complex responses in other muscles. Thus, the effect on timing could not be completely accounted for by loading of the limb itself and may involve other factors related to the control of equilibrium and volitional responses (Misiaszek et al. 2000). One way these factors can be eliminated is by using human infants. Infants provide a means to study human stepping with minimal interference from descending input and postural responses

(Forssberg 1985). A recent study has shown that phasic sensory cues such as unloading of the support limb or extension of the hip joint are strong stimuli for the initiation of the swing phase, similar to that reported in reduced preparations of the cat (Pang and Yang 2000). Developmental changes, the nature of bipedal walking, and volitional responses may be factors that account for the differences in the results obtained from cats and adult humans.

1.5.2 Afferent Regulation of the Magnitude of Extensor Burst Activity

Proprioceptive input plays an important role in regulating the magnitude of extensor activity during locomotion. One demonstration of this comes from a series of 'foot-in-hole' experiments in cats (Gorassini et al. 1994; Hiebert et al. 1994, Hiebert et al. 1995). With the unexpected loss of ground support, there is a shortening of extension and a marked reduction in the magnitude of extensor activity before the limb is lifted out of the hole (Gorassini et al. 1994). Hiebert et al. (1994) proposed that these responses were due to the lack of Ia and Ib afferent activity from extensor muscles that should normally reinforce extensor muscle activity during stance. Evidence for this proposal was later obtained by Hiebert et al. (1995) who showed that the corrective response was suppressed and extensor activity was maintained with electrical stimulation of extensor group I muscle afferents delivered when the foot entered the hole, thus indicating that feedback from extensor group I afferents reinforces extensor activity during locomotion. This conclusion supported previous findings that stimulation of extensor group I afferents enhanced the amplitude of extensor bursts during stance in spinal (Conway et al. 1987; Gossard et al. 1994) and decerebrate cats (Guertin et al. 1995; McCrea et al. 1995).

More recently, the extent to which afferent feedback contributes to extensor activity during walking has been examined quantitatively. In clonidine-treated acute spinal cats, Bennett et al. (1996) estimated that reflexes contribute, on average, 23% of the force due to stretch in the ankle extensor muscles during locomotion. Using a variety of approaches, Hiebert and Pearson (1999) estimated that between 50 and 80% of knee and ankle extensor activity is produced by afferent feedback during walking in decerebrate cats. First, the overall contribution of afferent feedback to extensor burst activity during locomotion was estimated by measuring the reduction in ankle and knee extensor activity during the 'foot-in-hole' trials. Electromyographic (EMG) activity in these muscles was reduced by about 70%. If the ankle extensors were loaded as the leg entered the hole, the reduction in extensor activity was prevented. Second, unloading of the hindlimbs (by lifting the hindquarters) during treadmill locomotion resulted in a large decrease in the magnitude of knee extensor EMG. Finally, transection of the dorsal roots that carry afferent input from the knee extensor muscles resulted in a reduction of knee extensor muscle activity by about 50%. Transection of more caudal dorsal roots that carry afferent input from ankle extensor muscles resulted in a reduction of ankle and knee extensor activity by 50 to 80%.

In a subsequent study, Stein et al. (2000) quantified the contribution of reflexes, evoked by phasic length changes of the ankle extensors, to the force generated by the ankle extensor muscles during the stance phase. In walking decerebrate cats, one hindlimb was immobilized and the triceps surae muscles were attached to a mechanical puller. With this puller, the triceps surae could either be held at a constant length or made to go through the changes in length that occur normally during the E2 and E3 phases of locomotion during walking. By using this approach and comparing muscle forces with the forces generated in deafferented triceps surae muscles, it was estimated that 35% of the force generated in ankle extensors during stance comes from feedback related to length changes that occur during walking.

The importance of afferent feedback from extensor muscles in regulating extensor burst magnitude during stance has also been shown in humans. In both healthy and spinal cord injured human adults, afferent feedback during the stance phase of locomotion contributes to the magnitude of extensor activity (Yang et al. 1991; Harkema et al. 1997; Stephens and Yang 1999; Sinkjaer et al. 2000). Sinkjaer et al. (2000) reported that up to 50% of soleus muscle activity during the stance phase of human walking is due to afferent feedback. When the ankles were unloaded (using a motorized mechanical joint strapped around the ankle) during treadmill walking, a significant reduction (50%) in soleus EMG activity was observed (Sinkjaer et al. 2000). Grey et al. (2001) suggested that group II afferents contribute to the magnitude of soleus EMG during the stance phase in human walking. Their conclusions were based on the fact that the medium-latency component of the stretch reflex response evoked during the stance phase was not influenced by ischemic block of soleus Ia afferents. In addition, after subjects ingested tizanidine (a drug known to depress transmission in group II afferent pathways), the medium-latency component of the corrective response to ankle extensor stretch during the stance phase was depressed (Grey et al. 2001). It is not known whether tizanidine has an effect on Ib afferent pathways, so the possibility that load-sensitive afferents also contribute to the medium-latency stretch reflex response has not been excluded (Grey et al. 2001).

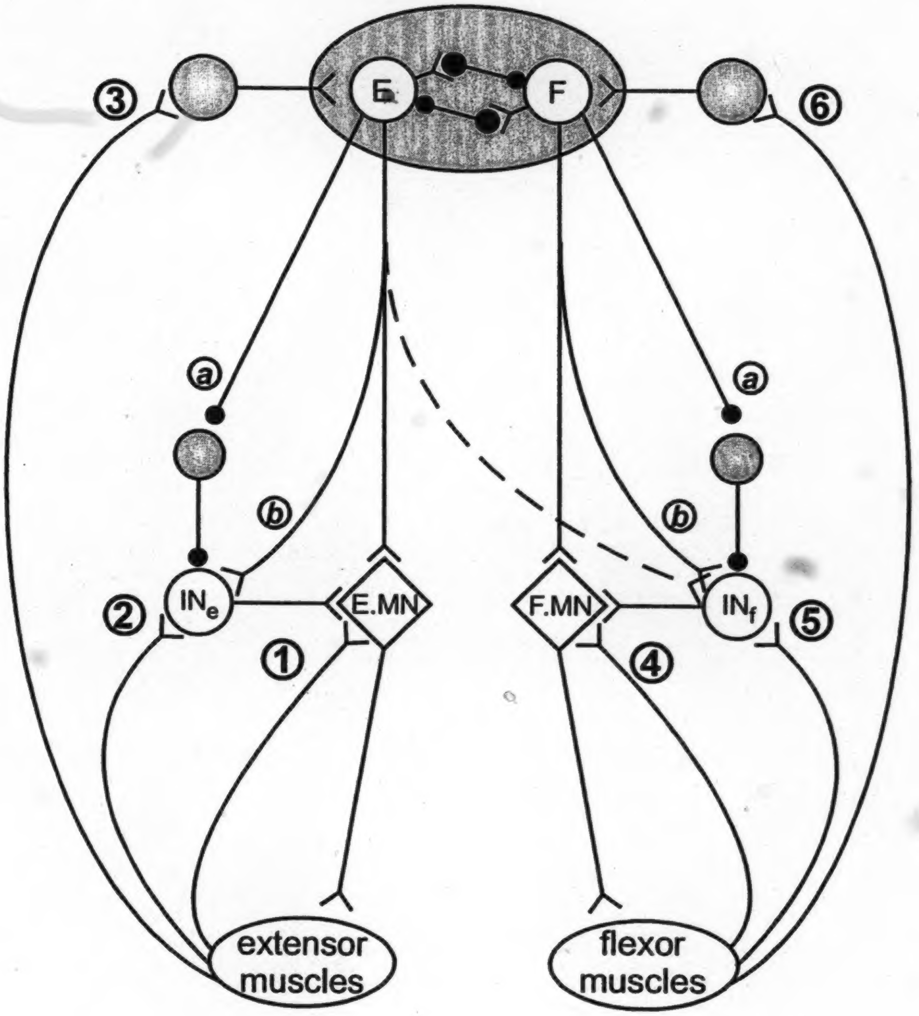
1.5.3 Segmental Pathways Involved in the Afferent Regulation of Extensor Burst Activity

With the demonstration that proprioceptive feedback regulates the timing and magnitude of extensor activity during locomotion, an important issue is the identity of the segmental reflex pathways by which these afferents exert their action on the locomotor system. It is now apparent that multiple pathways are involved in shaping the output of the locomotor CPG and that input from different afferents converge onto interneurons thus yielding common effects on locomotor activity. In addition, transmission in many of these reflex pathways is modulated in a task- and phase-dependent manner (reviewed in McCrea 2001). For example, the inhibitory influence from group Ib extensor afferents to extensor motoneurons becomes excitatory during locomotion (Pearson and Collins 1993; McCrea et al. 1995).

Figure 1.1 illustrates the various pathways by which muscle afferents affect the locomotor output. As shown in the left side of figure 1.1, extensor group I afferents can exert their effects on extensor motoneurons by at least three pathways. First, extensor muscle afferents can exert a direct effect on extensor motoneurons via the well-known group Ia monosynaptic pathway (Eccles et al. 1957) (*pathway 1*, Fig. 1.1). Second, extensor group I muscle afferents can excite extensor motoneurons via disynaptic excitatory pathways (McCrea et al. 1995; Angel et al. 1996) (*pathway 2*, Fig. 1.1). A feature of this disynaptic excitatory pathway is that it is open only during locomotion (McCrea et al. 1995; Angel et al. 1996). The locomotor-dependent disynaptic excitatory connection may be

Figure 1.1. Muscle Afferent Pathways Regulating Extensor and Flexor Activity during Locomotion.

Excitatory connections are represented by inverted arrows and inhibitory connections by black dots. The locomotor CPG is represented by the network contained in the grey shaded ellipse (E, extensor half-centre; F, flexor half-centre). Shaded circles represent putative interneuron(s) in the connections made to and from the locomotor CPG. Interneurons IN_e and IN_f are the interposed interneurons in the identified disynaptic reflex pathway from extensor and flexor group I afferents to extensor and flexor motoneurons, respectively. Extensor (E.MN) and flexor motoneurons (F.MN) are represented by diamonds. Pathways 1 and 4 are the monosynaptic pathway from group Ia afferents to their respective motoneurons. Pathways 2 and 5 represent the disynaptic pathway from group I afferents to the motoneurons. Pathways 3 and 6 represent muscle afferent pathways which directly affect the locomotor CPG (adapted and modified from McCrea 2001; Quevedo et al. 2000; Pearson 1995). See text for further details.


E
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extensor muscles
flexor muscles

opened by either a disinhibition (*pathway a*, Fig. 1.1) or excitation from the extensor half-centre (*pathway b*, Fig. 1.1) of the intervening interneuron (IN_e in Fig. 1.1). Recently, an interneuron population that may mediate the disynaptic excitation of extensor motoneurons during locomotion was identified (McCrea et al. 2001). These interneurons are located in laminae 4-6 and close to the motoneurons to which they project (see McCrea 2001). A third pathway by which extensor group I afferents can shape locomotor output is by direct action onto the locomotor CPG (*pathway* 3, Fig. 1.1). The ability for a given stimulus to reset or entrain the locomotor rhythm is evidence for its effect on the locomotor CPG (Hultborn et al. 1998). As discussed in the preceding sections, activation of extensor group I afferents by various stimuli (e.g. large amplitude ramp stretches, force pulses, electrical stimulation) entrains the locomotor rhythm (Conway et al. 1987, Pearson et al. 1992, Gossard et al. 1994) and also prolongs the duration of extensor activity (Guertin et al. 1995; Whelan et al. 1995a). The fact that activation of primary and secondary muscle spindles from flexor muscles also resets the locomotor rhythm indicates a pathway from these afferents to locomotor CPG (Perreault et al. 1995; Hiebert et al. 1996) (*pathway* 6, Fig. 1.1).

1.5.4 Afferent Regulation of the Timing and Magnitude of Flexor Burst Activity

An important issue in the regulation of swing phase activity during walking is how the nervous system ensures that the trajectory of the limb and subsequent foot placement in preparation for support is accurately achieved. The significant role of cutaneous afferents (reviewed in Rossignol 1996) and supraspinal control (reviewed in Drew et al. 1996) during the swing phase has been established. The first evidence for the influence of proprioceptive feedback during the swing phase of locomotion came from the experiments of Orlovskii and Shik (1965). During treadmill locomotion in dogs they found that when a braking force was applied to the forelimb at the elbow, the forelimb was able to quickly compensate (within 30 ms) and resume forward movement with the same speed and inter-joint coordination as during control steps. The short time delay of the compensatory response led Orlovskii and Shik (1965) to conclude that segmental mechanisms exist that monitor and appropriately respond to changes in proprioceptive input during the swing phase. Similarly, in humans, Garrett and Luckwill (1983) reported that a mechanical perturbation during the swing phase of treadmill locomotion caused a shift in the timing of EMG activity while preserving angular velocity of the knee joint. Thus, they concluded that proprioceptive inputs, triggered by the mechanical perturbation, function to stabilize movement of the knee and thereby ensure stability of the body during the swing phase.

Recently, more evidence for the functional importance of proprioceptive input during the swing phase of walking has emerged. It is now apparent that, as in the extensor system, both the timing and magnitude of flexor activity are regulated by proprioceptive feedback from receptors in flexor muscles. This was clearly demonstrated in a recent study in decerebrate walking cats (see Chapter 3, Lam and Pearson 2001a). Although the specific receptors controlling flexor burst activity in these experiments could not be identified, the results suggest that Golgi tendon organs and muscle spindles could be important receptors for monitoring the load and length changes imposed on the muscles during the various perturbations. Indeed, a significant advance over the past few years has been the accumulation of direct information on the role of feedback from these large muscle afferents in regulating the duration and magnitude of flexor activity during locomotion.

During fictive locomotion in decerebrate cats, stimulation of group I afferents from TA, extensor digitorum longus (EDL), IP, sartorius, and posterior biceps and semitendinosus (PbST) during the flexion phase generally resulted in a prolongation of flexor bursts, although the effects from TA stimulation were variable (Perreault et al. 1995; McCrea et al. 2000). In the case of sartorius group I afferent stimulation, a prolongation of the step cycle duration was also produced (Perreault et al. 1995). Additionally, stimulation of group I muscle afferents from the IP and sartorius muscles enhances the magnitude of flexor bursts (McCrea et al. 2000).

Because stimulation of muscle afferents at group I strengths recruits afferents from both muscle spindles and Golgi tendon organs, the relative contribution of Ia and Ib afferents to flexor motoneuron activation during locomotion is presently unclear. A role for Ia afferents is likely since small stretches to the EDL muscle produced disynaptic excitation of EDL and TA motoneurons, similar to that obtained with electrical stimulation (Quevedo et al. 2000). On the other hand, stretch of the IP tendon during flexion produced little effect on cycle period or flexor burst duration (Hiebert et al. 1996; Lam and Pearson 2001a). Thus, the extent to which group I flexor muscle afferents have an effect on the locomotor pattern appears to depend on the muscle from which these afferents arise.

The influence of feedback from flexor group II muscle afferents on the flexor phase of locomotion has also been investigated (Perreault et al. 1995; McCrea et al. 2000). Thus far, the findings have been inconsistent. Initially, Perreault et al. (1995) reported that stimulation of TA, PbST, and sartorius nerves at group II strength during flexion reset the locomotor rhythm to extension during fictive locomotion in decerebrate cats. More recently however, McCrea et al. (2000) found that during flexion, stimulation of group II muscle afferents from EDL, IP, and sartorius prolonged the duration and enhanced the magnitude of flexor activity while stimulation of group II afferents from TA reset the locomotor rhythm to extension. Activation of group II afferents from the EDL and TA muscles also prolongs flexor burst duration in walking decerebrate cats (Hiebert et al. 1996). The inconsistency between reports of the action of group II muscle afferents may be partly explained by recent findings (see Chapter 4, Lam and Pearson 2001b). During treadmill walking of decerebrate cats, group II stimulation of sartorius muscle afferents during flexion initially resulted in inhibition of IP bursts (decreased IP magnitude) followed by a resetting of the locomotor rhythm. However, with prolonged exposure to this stimulus (>5 trials), this inhibitory effect was suppressed and an excitatory response on IP burst duration and amplitude emerged (Lam and Pearson 2001b). Thus, it appears that the time-course and history of exposures to group II stimulation should be taken into account when considering the influence of group II flexor muscle afferents on locomotor activity and rhythm.

The effects of group I and II flexor muscle afferent stimulation on flexor activity during the swing phase of decerebrate cat locomotion could account for the effects observed in conscious cats undertaking different walking tasks. For example, in cats walking uphill, hip flexor muscles produce greater activity during the swing phase (Carlson-Kuhta et al. 1998). In both intact cats and humans, greater flexor activity is also required in order to step over obstacles (Lavoie et al. 1995; McFadyen and Carnahan 1997; McFadyen et al. 1999). These increases in flexor activity could be mediated by increased Golgi tendon organ activity due to loading of the flexor muscles as the leg has to move more against gravity. Another example comes from unpublished observations that the addition of an extra load strapped around a cat's hindlimb results in greater flexor burst magnitude and duration during the swing phase of treadmill locomotion (Lam and Pearson, unpublished data) and greater flexor muscle torque, particularly at the knee, during obstacle avoidance (see Chapter 5). Thus, feedback from Golgi tendon organs could be functionally important in situations where greater force generation is required in flexor muscles.

1.5.5 Segmental Pathways Involved in the Afferent Regulation of Flexor Burst Activity

The identity of the segmental pathways by which muscle afferents from flexor muscles exert an effect on flexor motoneurons during locomotion is beginning to be addressed. Data available so far indicate that the regulation of flexor burst activity by flexor group I afferent pathways bears a close resemblance to those from extensor afferents regulating extensor burst activity during locomotion (Fig. 1.1). Afferent feedback from flexors influences both the timing and magnitude of flexor burst activity by direct action on flexor motoneurons (Lundberg 1981, Quevedo et al. 2000) (*pathway* 4, Fig. 1.1), by disynaptic excitatory pathways to flexor motoneurons (Degtyarenko et al. 1998; Quevedo et al. 2000) (*pathway* 5, Fig. 1.1), and by direct action on the locomotor pattern generator (Perreault et al. 1995; McCrea et al. 2000) (*pathway* 6, Fig. 1.1). Other similarities are convergence of different afferent inputs to produce common effects and reorganization of reflex pathways in a state-dependent manner. For example, the switch from an inhibitory to an excitatory connection in the disynaptic pathway from flexor group I afferents to flexor motoneurons is an example of reflex reorganization that occurs in the presence of locomotion (Quevedo et al. 2000). Disynaptic excitatory pathways from flexor group I afferents to flexor motoneurons are opened during locomotion (via *pathways a and b* onto IN_f in Fig. 1.1) but not at rest, with transmission strongest during the flexion phase and only weakly present during the extension phase (indicated by dotted line in Fig. 1.1). In addition, the pathways appear to provide input mainly to homonymous motoneurons. Input to synergists is present, but to a lesser extent (Quevedo et al. 2000).

1.6 Adaptive Plasticity in the Walking System

Afferent feedback is also important for the adaptive modification of the locomotor system after changes or injury to the musculoskeletal or nervous system. The previous sections highlighted the importance of afferent pathways in regulating the motor output during locomotion and the significant advances that have been made in the identification of the pathways by which afferent feedback shapes locomotor output. The important concept is that proprioceptive inputs provide cues about the mechanical state of the musculoskeletal apparatus and this information is used to control the timing and magnitude of motor activity. One implication of this concept is that proprioceptive signals can also provide information about persistent changes in the mechanical properties of the system and therefore be used to adapt the motor output to meet the requirements of the altered limb mechanics. Since the musculoskeletal properties of the leg change throughout life, mechanisms must be in place for matching the motor output with current leg mechanics. This concept provided the basis for the final 2 projects of this thesis (see Chapters 5 and 6).

1.6.1 Adaptive Modifications to Locomotion in Cats after Peripheral Nerve Injury

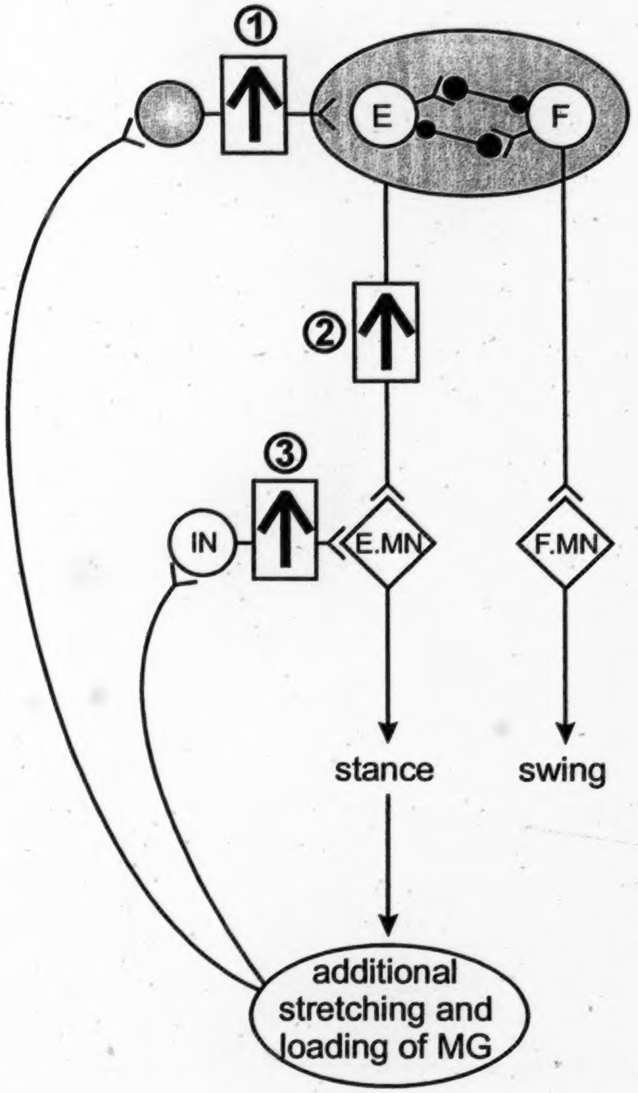
The first indication that adaptive plastic changes occur in the reflex pathways that regulate locomotor output came from studies on the influence of group I afferents on extensor duration (Whelan et al. 1995b, 1997). An interesting feature of the regulation of extensor burst duration by group I afferents from the ankle extensor muscles is that there is an imbalance in the relative contribution of afferents from different muscles. Stimulation of group I afferents from the LGS nerve is normally more effective than stimulation of group I afferents from the medial gastrocnemius (MG) nerve for regulating extensor burst duration during stance (Whelan et al. 1995a). After sectioning all of the ankle extensor nerves, except those from MG, the effectiveness of MG nerve stimulation became stronger in the days following the neurectomy and was able to exert a more powerful effect on extensor burst duration (Whelan et al. 1995b, Whelan and Pearson 1997). The increase in efficacy of MG nerve stimulation on modifying extensor burst duration is most likely mediated by an increased gain in the pathway from MG group I afferents to the locomotor CPG (Whelan and Pearson 1997) (*pathway 1*, Fig. 1.2).

Denervation of the synergists to MG also caused a progressive adaptive increase in the magnitude of MG activity during walking (Pearson et al. 1999; Pearson and Misiaszek 2000). The increase in the late component of MG EMG (which is centrally and peripherally driven) occurred rapidly, within the first few days after denervation (Pearson et al. 1999). On the other hand, the magnitude of the early component of MG EMG (which is centrally driven) increased gradually over a 1-week period (Pearson et al. 1999). Both of these adaptive increases were correlated with functional improvement, as indicated by a decrease in the amount of ankle flexion during stance. The differential time course of recovery between the early and late components of MG EMG indicates separate mechanisms that mediate the adaptive increases in MG activity. Since the early component is generated by central mechanisms (Gorassini et al. 1994), the gradual increase in this component of MG EMG is likely mediated by an increase in central drive (*pathway* 2, Fig. 1.2) (Pearson et al. 1999; Gritsenko et al. 2001).

What are the mechanisms that underlie the rapid adaptive increase in the late component of MG EMG after denervation of MG synergists? Pearson and Misiaszek (2000) found a use-dependent increase in the slope of the relationship between MG magnitude and the amount of yield (flexion) at the ankle during stance. These observations are consistent with the idea that an increase in gain of the reflex pathways from MG afferents to MG motoneurons occurs after denervation of MG synergists (Pearson et al. 1999; Pearson and Misiaszek 2000). Although other sources of afferent input cannot be discounted, this increase in gain is likely primarily driven by the greater afferent input from the isolated MG muscle since the adaptive responses are not present if the ankle is immobilized after the neurectomy (Pearson et al. 1999). The adaptive increase in the magnitude of MG EMG could be due to facilitation of disynaptic reflex pathways from extensor group I afferents to MG motoneurons (*pathway* 3, Fig. 1.2). On the other hand, Gritsenko et al. (2001) contend that the adaptive increase in the late component of MG EMG after neurectomy could be accounted for by an increase in central drive. This conclusion was based on the fact that the increase in the initial component of MG EMG occurred in proportion to an increase in the MG stretch reflex response, thereby indicating that the adaptive increase in the stretch reflex was due to higher levels of central drive to MG motoneurons (Gritsenko et al. 2001). Methodological differences could account for the different conclusions made by Gritsenko et al. (2001) and Pearson and Misiaszek (2000). Gritsenko et al. (2001) commenced post-denervation recordings after 12 hours, during which time the cats were free to move about in their cages while Pearson et al. (1999)

Figure 1.2. Adaptive Modifications of the Locomotor Pattern following Partial Denervation of Ankle Extensors.

Schematic diagram of central and reflex pathways from MG group I afferents that regulate extensor activity during locomotion. Abbreviations and symbols are in the same convention as in figure 1.1. After LGS and plantaris denervation, adaptive increases in MG activity occur via an increase in the influence in the oligosynaptic pathway from group I afferents to the locomotor CPG (1), an increase in the central drive from the locomotor CPG to extensor motoneurons (2), and an increase in reflex activation of extensor motoneurons via the disynaptic excitatory pathway (3).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commenced post-denervation recordings after only 5 hours, during which time the cats were confined to a small kennel, allowing little movement. The largest increases in the magnitude of the late component were observed by Pearson et al. (1999) to occur early in the recovery phase. Thereafter, the magnitudes of the early and late components increased relatively in proportion, similar to the findings of Gritsenko et al. (2001). The combination of allowing the animals to exercise after the denervation coupled with a slightly longer time delay before the first recordings were made could account for Gritsenko et al. (2001) finding no evidence for an independent increase in the gain of stretch reflex pathways not associated with an increase in central drive.

After denervations of the LGS muscles, chronic spinal cats also show similar functional improvement (decreased ankle flexion during stance) as observed in intact cats (Bouyer et al. 2001). This further indicates that neural mechanisms at the spinal level can detect and make compensations for deficits induced by ankle extensor neurectomy. However, chronic spinal cats do not consistently show the differential time course of adaptive increase in the early- and late-components of MG EMG. Furthermore, the increased effectiveness of electrical stimulation of MG group I muscle afferents on extensor burst duration seen in intact cats (Whelan and Pearson 1997) does not necessarily occur in chronic spinal cats after neurectomy (Bouyer et al. 2001). Thus, it remains unclear whether the mechanisms used by chronic spinal cats to recover function after neurectomy are the same as those used by intact cats.

Evidence that plasticity in descending input from supraspinal centres may play a role in the adaptive modifications that occur in intact cats comes from the experiments conducted by Carrier et al. (1997). They showed that conscious cats were able to adapt their locomotor pattern very well following a neurectomy of the ankle flexors TA and EDL. The adaptation consisted of small increases in knee and hip flexor activity allowing the paw to clear the ground during the swing phase. After spinalization, however, the locomotor pattern deteriorated with the increase in hip and knee flexion greatly exaggerated and the appearance of other abnormal movement patterns. Even with training, the locomotor pattern did not improve. If spinalization is performed before denervation of the TA and EDL and the cats are step-trained, minimal effects on the locomotor pattern are seen. That is, the spinal cats could make appropriate modifications to compensate for the denervation similar to that seen in uninjured cats. This difference in the locomotor recovery between spinalization following denervation and denervation following spinalization implies that the plasticity in response to denervation alone involves modifications at both the spinal and supraspinal levels. Removal of supraspinal input after denervation reveals unorganized movements generated by the plasticity at the spinal level (Carrier et al. 1997).

1.6.2 Adaptive Modifications to Locomotion after Biomechanical Changes to the Limb

Throughout an organism's development and growth, changes to the physical properties of the limbs inevitably occur and adaptive processes must be available to respond to these changes, which are not necessarily initiated by nerve injury (Pearson 2000). Thus, an important issue is to address the question of how adaptive modifications occur in response to training or alterations in the biomechanical properties of the limb.

To address this issue in the ankle extensor system of walking cats, Misiaszek and Pearson (2002) studied the effects of weakening the ankle extensor muscles (except MG) with injections of botulinum toxin on the locomotor pattern in normal cats. Similar to the response to ankle extensor nerve transection (Pearson et al. 1999), injection of botulinum toxin into the ankle extensor muscles induced a progressive increase in MG burst amplitude. Furthermore, this initial adaptive increase in MG activity was sufficient to respond to subsequent events that weakened the ankle extensor muscle group (a second botulinum toxin injection and final nerve cut to ankle extensor nerves) (Misiaszek and Pearson 2002).

There are numerous other examples of adaptation in the locomotor system in response to a sustained alteration in the biomechanics of the limb or external conditions (reviewed in Pearson 2000). During treadmill locomotion, decerebrate ferrets can be conditioned to increase the height of their forelimb trajectory to step over an obstacle (Lou and Bloedel 1988). Adaptation occurred rapidly, after as few as 7 perturbation trials during which the obstacle (a straight rod) was placed in the trajectory of the swinging forelimb. Upon removal of the obstacle, the conditioned increase in paw trajectory persisted for a few steps before returning to control levels.

In humans, evidence for learning in a variety of locomotor tasks is also observed. For example, after a period of walking on a rotating disk, humans will continue to walk along a curved trajectory when asked to walk in a straight line over level ground with their eyes closed (Gordon et al. 1995; Weber et al. 1998). Similarly, after a period of jogging on a treadmill, subjects will inadvertently jog forwards over level ground when asked to jog in-place with their eyes closed (Anstis 1995). Similar results were obtained for hopping on one leg on the treadmill. After dismounting the treadmill, subjects also hopped forward on the same leg when asked to hop in-place with their eyes closed (Anstis 1995). This after-effect was not observed with the opposite leg suggesting that peripheral rather than central mechanisms were involved in the adaptation. Similarly, adaptation to walking on a split-belt treadmill also does not transfer between the two legs (Prokop et al. 1995). After the initial adaptation to walking on a split-belt treadmill, the relative speeds of the two treadmill belts were switched. Adaptation to this "mirror condition" required the same amount of time as the initial adaptation. Thus, learning in the lower limbs appears to be dependent on specific proprioceptive input from the perturbed limb.

A further issue that remains to be resolved is the sites within the nervous system where plastic changes responsible for mediating the adaptation to locomotor activity are located. Several lines of evidence indicate that the cerebellum is involved in motor learning of upper limb movements (Kitazawa et al. 1998; Thach 1998; Imamizu et al. 2000; Nezafat et al. 2001) and eye movements (Gomi et al. 1998). The cerebellum also appears to have a similar role during learning of locomotor tasks (Yanagihara and Kondo 1996; Rand et al. 1998). Yanagihara et al. (1993) showed that chronic decerebrate cats could adapt slowly to different treadmill speeds on a split-belt treadmill. During this perturbed locomotion, increases in climbing fiber discharges from Purkinje cells in the cerebellum were recorded (Yanagihara and Udo 1994). Furthermore, inactivation of nitric oxide pathways, which are involved in long-term depression in Purkinje cells in the cerebellum, abolished motor learning in decerebrate cats walking on split-belt treadmill (Yanagihara and Kondo 1996). These sets of data provide compelling support for the idea that cerebellar pathways are important for mediating adaptations during locomotor tasks. In humans, similar support for the role of the cerebellum for motor learning during locomotion has been provided by Rand et al. (1998). They showed that subjects with cerebellar lesions employed more variable and inefficient compensatory patterns in response to perturbations to treadmill speed compared with healthy subjects. The nature of these compensations were consistent with the incapacity of cerebellar patients to adequately respond to on-line processing of sensory information (temporal and proprioceptive) and inadequate scaling of the magnitude of motor movements (Rand et al. 1998). Thus, although the cerebellar patients could adapt their locomotor pattern to perturbations in treadmill speed, the lack of consistency and efficiency seen in their response patterns suggests the need for an intact cerebellum for the complete adaptive pattern seen in normal controls.

1.7 Summary and Thesis Objectives

This introductory section has reviewed the present state of knowledge regarding the adaptive control of locomotion with special focus on issues pertaining to the possibility of shared neural circuitry for locomotion, the proprioceptive regulation of locomotion, and the involvement of these afferents in long-term adaptive modifications to the locomotor pattern that take place after injury and persistent changes to limb mechanics and external conditions. Valuable information on the malleability of pattern-generative networks has come from invertebrate and simple vertebrate preparations and provided a framework for investigations of similar flexibility in mammalian locomotor networks. While our understanding of the intricate organization of mammalian locomotor-generating circuits is far less detailed than that of simpler organisms, behavioural evidence has provided some insight into the possibility that shared circuitry exists between various locomotor tasks as well as with other rhythmic behaviours. Additional insight into the organization of locomotor generating networks has been provided by the substantial progress made in the identification of the afferents and their segmental pathways involved in the regulation of locomotor activity, particularly those regulating stance phase activity. The identification of the interneurons interposed in these afferent pathways is beginning to occur. Further work is needed to elucidate the specific afferents and their pathways in the regulation of swing phase activity. Nevertheless, data available so far indicate that the pathways are analogous to those regulating the stance phase. Together, data on the afferent regulation of extensor and flexor activity provide an important framework for examining the mechanisms underlying adaptive modifications of locomotor activity in response to changes in the nervous or musculoskeletal systems. Indeed, it has been found that some of the same pathways that regulate extensor activity during locomotion can also undergo changes in gain to compensate for changes in the neuromuscular apparatus of the lower leg. Knowledge of the reflex pathways that regulate locomotor output and their role in adaptive modifications after injury have important implications for the development and improvement of artificial control systems as well as rehabilitative techniques in individuals after central and peripheral nervous system injury.

The projects presented in this thesis focus on 3 areas related to the adaptive control of locomotion. The first project examined the concept of shared neural networks for the control of different directions of locomotion and found evidence consistent with the idea for a common locomotor pattern generator for all directions of human infant stepping (Chapter 2). The second project investigated the role of proprioceptive input from hip flexor muscles in the regulation of flexor activity during the swing phase of decerebrate cat locomotion (Chapter 3). The data showed that proprioceptive input from the sartorius muscles was particularly important for regulating hip flexor amplitude and duration during the swing phase. Based on these results, the role of sartorius muscle afferents was investigated in more detail in a subsequent study by electrically stimulating the sartorius nerve at various strengths during treadmill locomotion in decerebrate cats (Chapter 4). The demonstration that proprioceptive feedback is important for regulating the activity of flexor muscles inevitably led to the question of whether sustained changes to proprioceptive feedback mediates long-term adaptive modifications during the swing phase of cat locomotion. This issue was investigated in the final studies that examined the adaptations that occurred in response to loading of the limb during the swing phase of stepping in intact cats (Chapter 5) and human infants (Chapter 6).

1.8 References

Andersson O, Grillner S. Peripheral control of the cat's step cycle. II. Entrainment of the central pattern generators for locomotion by sinusoidal hip movements during "fictive locomotion". *Acta Physiologica Scandinavica* 118: 229-239 1983.

Angel MJ, Guertin P, Jimenez T, McCrea DA. Group I extensor afferents evoke disynaptic EPSPs in cat hindlimb extensor motoneurones during fictive locomotion. *Journal of Physiology* 494: 851-861 1996.

Anstis S. Aftereffects from jogging. *Experimental Brain Research* 103: 476-478, 1995.

Barkovich AJ, Kjos BO, Jackson DE, Norman D. Normal maturation of the neonatal and infant brain: MR imaging at 1.5T. *Radiology* 166: 173-180, 1988.

Bekoff A. Neuroethological approaches to the study of motor development in chicks: achievements and challenges. *Journal of Neurobiology* 23: 1486-1505, 1992.

Bennett DJ, DeSerres SJ, Stein RB. Gain of the triceps surae stretch reflex in decerebrate and spinal cats during postural and locomotor activities. *Journal of Physiology* 496: 837-850, 1996.

Bouyer LJG, Whelan PJ, Pearson KG, Rossignol S. Adaptive locomotor plasticity in chronic spinal cats after ankle extensors neurectomy. *Journal of Neuroscience* 21: 3531-3541, 2001.

Brody BA, Kinney HC, Kloman AS, Gilles FH. Sequence of central nervous system myelination in human infancy. I. An autopsy study of myelination. *Journal of Neuropathology and Experimental Neurology* 46: 283-301, 1987.

Brown T. G. The intrinsic factors in the act of progression in the mammal. *Proceedings of the Royal Society of London Series B* 84: 308-319, 1911.

Buford JA, Smith JL. Adaptive control for backward quadrupedal walking. II. Hindlimb muscle synergies. *Journal of Neurophysiology* 64: 756-766, 1990.

Bussel B, Roby-Brami A, Azouvi P, Biraben A, Yakovleff A, Held JP. Myoclonus in a patient with spinal cord transection. *Brain* 111: 1235-1245, 1988.

Bussel B, Roby-Brami A, Yakovleff A, Bennis N. Late flexion reflex in paraplegic patients. Evidence for a spinal stepping generator. *Brain Research Bulletin* 22: 53-56, 1989.

Calancie B, Needham-Shropshire B, Jacobs P, Willer K, Zych G, Green BA. Involuntary stepping after chronic spinal cord injury. Evidence for a central rhythm generator for locomotion in man. *Brain* 117: 1143-1159, 1994.

Carlson-Kuhta P, Trank TV, Smith JL. Forms of forward quadrupedal locomotion. II. A comparison of posture hindlimb kinematics and motor patterns for upslope and level walking. *Journal of Neurophysiology* 79: 1687-1701, 1998.

Carrier L, Brustein E, Rossignol S. Locomotion of the hindlimbs after neurectomy of ankle flexors in intact and spinal cats: model for the study of locomotor plasticity. *Journal of Neurophysiology* 77: 1979-1993, 1997.

Carter MC, Smith JL. Simultaneous control of two rhythmical behaviors. I. Locomotion with paw-shake response in normal cat. *Journal of Neurophysiology* 56: 171-183, 1986a.

Carter MC, Smith JL. Simultaneous control of two rhythmical behaviors. II. Hindlimb walking with paw-shake response in spinal cat. *Journal of Neurophysiology* 56: 184-195, 1986b.

Choa BHG, Stephens JA. Cutaneous reflex responses and central nervous lesions studied in the lower limb in man. *Journal of Physiology* 328: 23P-24P, 1982.

Chugani HT, Phelps ME. Maturational changes in cerebral function in infants determined by ^{18}FDG positron emission tomography. *Science* 231: 840-843, 1986.

Connolly KJ, Forssberg H. Neurophysiology and neuropsychology of motor development. *Clinics in Developmental Medicine.* London, UK: Mac Keith Press, 1997.

Conway BA, Hultborn H, Kiehn O. Proprioceptive input resets central locomotor rhythm in the spinal cat. *Experimental Brain Research* 68: 643-656, 1987.

Dambska M, Kuchna I. Different developmental rates of selected brain structures in humans. *Acta Neurobiologiae Experimentalis* 56: 83-93, 1996.

Degtyarenko AM, Simon ES, Norden-Krichmar T, Burke RE. Modulation of oligosynaptic cutaneous and muscle afferent reflex pathways during fictive locomotion and scratching in the cat. *Journal of Neurophysiology* 79: 447-463, 1998.

DeVries JIP, Visser GHA, Prechtl HFR. Fetal motility in the first half of pregnancy. In: *Continuity of Neural Functions from Prenatal to Postnatal Life,* edited by HFR Prechtl. Oxford, UK: Spastics International Medical Publications, 1984, pp. 46-64.

Dickinson PS. Interactions among neural networks for behavior. *Current Opinion in Neurobiology* 5: 792-798, 1995.

Dietz V, Colombo G, Jensen L, Baumgartner L. Locomotor capacity of spinal cord in paraplegic patients. *Annals of Neurology* 37: 574-592, 1995.

Dimitrijevic MR, Gerasimenko Y, Pinter MM. Evidence for a spinal central pattern generator in humans. *Annals of the New York Academy of Sciences* 860: 360-376, 1998.

Drew T, Jiang W, Kably B, Lavoie S. Role of the motor cortex in the control of visually triggered gait modifications. *Canadian Journal of Physiology and Pharmacology* 74: 426-442, 1996.

Duysens J, Clarac F, Cruse H. Load-regulating mechanisms in gait and posture: comparative aspects. *Physiological Reviews* 80: 83-133, 2000.

Duysens J, Pearson KG. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Research* 187: 321-332, 1980.

Earhart GM, Stein PSG. Scratch-swim hybrids in the spinal turtle: blending of rostral scratch and forward swim. *Journal of Neurophysiology* 83: 156-165, 2000a.

Earhart GM, Stein PSG. Step swim and scratch motor patterns in the turtle. *Journal of Neurophysiology* 84: 2181-2190, 2000b.

Earhart GM, Jones GM, Horak FB, Block EW, Weber KD, Fletcher WA. Forward versus backward walking: transfer of podokinetic adaptation. *Journal of Neurophysiology* 86: 1666-1670, 2001.

Earhart GM, Jones GM, Horak FB, Block EW, Weber KD, Fletcher WA. Transfer of podokinetic adaptation from stepping to hopping. *Journal of Neurophysiology* 87: 1142-1144, 2002.

Eccles JC Eccles RM Lundberg A. The convergence of monosynaptic excitatory afferents on to many different species of alpha motoneurones. *Journal of Physiology* 137: 22-50, 1957.

Eidelberg E, Walden JG, Nguyen LH. Locomotor control in macaque monkeys. *Brain* 104: 647-663, 1981.

Engberg I, Lundberg A. An electromyographic analysis of muscular activity in the hindlimb of the cat during unrestrained locomotion *Acta Physiological Scandinavica* 75: 614-630, 1969.

Evans AL, Harrison LM, Stephens JA. Task-dependent changes in cutaneous reflexes recorded from various muscles controlling finger movement in man. *Journal of Physiology* 418: 1-12, 1989.

Eyre JA, Miller S, Ramesh V. Constancy of central conduction delays during development in man: investigation of motor and somatosensory pathways. *Journal of Physiology* 434: 441-452, 1991.

Fedirchuk B, Nielsen J, Petersen N, Hultborn H. Pharmacologically evoked fictive motor patterns in the acutely spinalized marmoset monkey (*Callithrix jacchus*). *Experimental Brain Research* 122: 351-361, 1998.

Forssberg H. Ontogeny of human locomotor control. I. Infant stepping supported locomotion and transition to independent locomotion. *Experimental Brain Research* 57: 480-493, 1985.

Garrett M, Luckwill RG. Role of reflex responses of knee musculature during the swing phase of walking in man. *European Journal of Applied Physiology* 52: 36-41, 1983.

Gibbs J, Harrison LM, Stephens JA. Cutaneomuscular reflexes recorded from the lower limb in man during different tasks. *Journal of Physiology* 487: 237-242, 1995.

Gomi H, Shidara M, Takemura A, Inoue Y, Kawano K, Kawato M. Temporal firing patterns of Purkinje cells in the cerebellar ventral paraflocculus during ocular following responses in monkeys. I. Simple spikes. *Journal of Neurophysiology* 80: 818-831, 1998.

Gorassini MA Prochazka A Hiebert GW Gauthier MJ. Corrective responses to loss of ground support during walking. I. Intact cats. *Journal of Neurophysiology* 71: 603-610, 1994.

Gordon CR, Fletcher WA, Jones GM, Block EW. Adaptive plasticity in the control of locomotor trajectory. *Experimental Brain Research* 102: 540-545, 1995.

Gossard J-P Brownstone RM Barajon I Hultborn H. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. *Experimental Brain Research* 98: 213-228, 1994.

Grey MJ, Ladouceur M, Andersen JB, Nielsen JB, Sinkjaer T. Group II muscle afferents probably contribute to the medium latency soleus stretch reflex during walking in humans. *Journal of Physiology* 534: 925-933, 2001.

Grillner S. Control of locomotion in bipeds, tetrapods, and fish. In: *Handbook of Physiology. Section 1: The Nervous System, Volume II. Motor Control, Part 2*, edited by JM Brookhart and VB Mountcastle. Bethesda, MD: American Physiological Society, 1981, pp. 1179-1236.

Grillner S, Rossignol S. On the initiation of the swing phase of locomotion in chronic spinal cats. *Brain Research* 146: 269-277, 1978.

Grillner S, Zangger P. How detailed is the central pattern generation for locomotion? *Brain Research* 88: 367-371, 1975.

Grillner S, Zangger P. On the central generation of locomotion in the low spinal cat. *Experimental Brain Research* 34: 241-261, 1979.

Grillner S, Zangger P. The effect of dorsal root transection on the efferent motor pattern in the cat's hindlimb during locomotion. *Acta Physiologica Scandinavica* 120: 393-405, 1984.

Gritsenko V, Mushahwar V, Prochazka A. Adaptive changes in locomotor control after partial denervation of triceps surae muscles in the cat. *Journal of Physiology* 533: 299-311, 2000.

Guertin P, Angel MJ, Perreault M-C, McCrea DA. Ankle extensor group I afferents excite extensors throughout the hindlimb during fictive locomotion in the cat. *Journal of Physiology* 487: 197-209, 1995.

Harkema SJ, Hurley SL, Patel UK, Requejo PS, Dobkin BH, Edgerton VR. Human lumbosacral spinal cord interprets loading during stepping. *Journal of Neurophysiology* 77: 797-811, 1997.

Hashimoto T, Tayama M, Miyazaki M, Kuroda Y. Development of the brainstem: assessment by MR imaging. *Neuropediatrics* 22: 139-146, 1991.

Hiebert GW, Gorassini MA, Jiang W, Prochazka A, Pearson KG. Corrective responses to loss of ground support during walking. II. Comparison of intact and chronic spinal cats. *Journal of Neurophysiology* 71: 611-622, 1994.

Hiebert GW, Pearson KG. Contribution of sensory feedback to the generation of extensor activity during walking in the decerebrate cat. *Journal of Neurophysiology* 81: 758-770, 1999.

Hiebert GW, Whelan PJ, Prochazka A, Pearson KG. Suppression of the corrective response to loss of ground support by stimulation of extensor group I afferents. *Journal of Neurophysiology* 73: 416-420, 1995.

Hiebert GW, Whelan PJ, Prochazka A, Pearson KG. Contribution of hind limb flexor muscle afferents to the timing of phase transitions in the cat step cycle. *Journal of Neurophysiology*

75: 1126-1137, 1996.

Holland BA, Haas DK, Norman D, Brant-Zawadzki M, Newton TH. MRI of normal brain maturation. *American Journal of Neuroradiology* 7: 201-208, 1986.

Humphrey T. The development of the pyramidal tracts in human fetuses, correlated with cortical differentiation. In: *Structure and Function of the Cerebral Cortex,* edited by DB Tower and JP Shade. Amsterdam: Elsevier Publishing Co., 1960, pp. 93-103.

Imamizu H, Miyauchi S, Tamada T, Sasaki Y, Takino R, Pütz B, Yoshioka T, Kawato M. Human cerebellar activity reflecting an acquired internal model of a new tool *Nature* 403: 192-195, 2000.

Issler HC, Stephens JA. The maturation of cutaneous reflexes studied in the upper limb in man. *Journal of Physiology* 335: 643-654, 1983.

Jankowska E, Jukes MGM, Lund S, Lundberg A. The effect of DOPA on the spinal cord. 5. Reciprocal organization of pathways transmitting excitatory action to alpha motoneurones of flexors and extensors. *Acta Physiological Scandinavica* 70: 369-388, 1967a.

Jankowska E, Jukes MGM, Lund S, Lundberg A. The effect of DOPA on the spinal cord. 6. Half-centre organization of interneurones transmitting effects from the flexor reflex afferents. *Acta Physiological Scandinavica* 70: 389-402, 1967b.

Jean A. Brain stem control of swallowing: neuronal network and cellular mechanisms. *Physiological Reviews* 81: 929-969, 2001.

Jenner JR, Stephens JA. Cutaneous reflex responses and their central nervous pathways studied in man. *Journal of Physiology* 333: 405-419, 1982.

Kitazawa S, Kimura T, Yin P-B. Cerebellar complex spikes encode both destinations and errors in arm movements. *Nature* 392: 494-497, 1998.

Koh THHG, Eyre JA. Maturation of corticospinal tracts assessed by electromagnetic stimulation of the motor cortex. *Archives of Disease in Childhood* 63: 1347-1352, 1988.

Kriellaars DJ, Brownstone RM, Noga BR, Jordan LM. Mechanical entrainment of fictive locomotion in the decerebrate cat. *Journal of Neurophysiology* 71: 2074-2086, 1994.

Lam T, Pearson KG. Proprioceptive modulation of hip flexor activity during the swing phase of locomotion in decerebrate cats. *Journal of Neurophysiology* 86: 1321-1332, 2001a.

Lam T, Pearson KG. Stimulation of group I and II sartorius muscle afferents during the swing phase of walking in decerebrate cats. *Society for Neuroscience Abstracts* 27: 1060, 2001b.

Lamb T, Yang JF. Could different directions of infant stepping be controlled by the same locomotor central pattern generator? *Journal of Neurophysiology* 83: 2814-2824, 2000.

Lavoie S, McFadyen B, Drew T. A kinematic and kinetic analysis of locomotion during voluntary gait modification in the cat. *Experimental Brain Research* 106: 39-56, 1995.

Leonard CT, Matsumoto T, Diedrich P. Human myotatic reflex development of the lower extremities. *Early Human Development* 43: 75-93, 1995.

Lieske SP, Thoby-Brisson M, Telgkamp P, Ramirez JM. Reconfiguration of the neural network controlling multiple breathing patterns: eupnea, sighs and gasps. *Nature Neuroscience* 3: 600-607, 2000.

Lou J-S, Bloedel JR. A new conditioning paradigm: conditioned limb movements in locomoting decerebrate ferrets. *Neuroscience Letters* 84: 185-190, 1988.

Lundberg A. Half-centres revisited. In: *Regulatory Functions of the CNS. Motion and Organization Principles, vol.1 Advances in Physiological Sciences*, edited by J Szentagothai, M Palkovits, and J Hamori. Budapest: Pergamon Press, 1981, pp. 155-167.

Marder E, Bucher D. Central pattern generators and the control of rhythmic movements. *Current Biology* 11: R986-R996, 2001.

Marder E, Calabrese RL. Principles of rhythmic motor pattern generation. *Physiological Reviews* 76: 687-717, 1996.

Matsushima T, Grillner S. Neural mechanisms of intersegmental coordination in lamprey: local excitability changes modify the phase coupling along the spinal cord. *Journal of Neurophysiology* 67: 373-388, 1992.

Mayer RF, Mosser RS. Maturation of human reflexes. Studies of electrically evoked reflexes in newborns, infants and children. In: *New Developments in Electromyography and Clinical Neurophysiology*, edited by JE Desmedt. Basel: Karger, 1973, pp. 294-307.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233, 2000.

McCrea DA, Shefchyk SJ, Stephens MJ, Pearson KG. Disynaptic group I excitation of synergist ankle extensor motoneurones during fictive locomotion in the cat. *Journal of Physiology* 487: 527-539, 1995.

McCrea DA. Spinal circuitry of sensorimotor control of locomotion. *Journal of Physiology* 533: 41-50, 2001.

McFadyen BJ, Carnahan H. Anticipatory locomotor adjustments for accommodating versus avoiding level changes in humans. *Experimental Brain Research* 114: 500-506, 1997.

McFadyen BJ, Lavoie S, Drew T. Kinetic and energetic patterns for hindlimb obstacle avoidance during cat locomotion. *Experimental Brain Research* 125: 502-510, 1999.

McGraw MB. Neuromuscular development of the human infant as exemplified in the achievement of erect locomotion. *Journal of Pediatrics* 17: 747-777, 1940.

Miller FR, Sherrington CS. Some observations on the bucco-pharyngeal stage of reflex deglutition. *Quarterly Journal of Experimental Physiology* 9: 147-186, 1916.

Misiaszek JE, Stephens MJ, Yang JF, Pearson KG. Early corrective reactions of the leg to perturbations at the torso during walking in humans. *Experimental Brain Research* 131: 511-523, 2000.

Misiaszek JE, Pearson KG. Adaptive changes in locomotor activity following botulinum toxin injection in ankle extensor muscles of cats. *Journal of Neurophysiology* 87: 229-239, 2002.

Müller K, Hömberg V, Lenard HG. Magnetic stimulation of motor cortex and nerve roots in children. Maturation of cortico-motoneuronal projections. *Electroencephalography and Clinical Neurophysiology* 81: 63-70, 1991.

Myklebust BM, Gottlieb GL, Agarwal GC. Stretch reflexes of the normal infant. *Developmental Medicine and Child Neurology* 28: 440-449, 1986.

Myklebust BM, Gottlieb GL. Development of the stretch reflex in the newborn: reciprocal excitation and reflex irradiation. *Child Development* 64: 1036-1045, 1993.

Nezafat R, Shadmehr R, Holcomb HH. Long-term adaptation to dynamics of reaching movements: a PET study. *Experimental Brain Research* 140: 66-76, 2001.

Nilsson J, Thorstensson A, Halbertsma J. Changes in leg movements and muscle activity with speed of locomotion and mode of progression in humans. *Acta Physiological Scandinavica* 123: 457-475, 1985.

Orlovskii GN, Shik ML. Standard elements of cyclic movement. *Biophysics* 10: 935-944, 1965.

Orsal D, Perret C, Cabelguen J-M. Evidence of rhythmic inhibitory synaptic influences in hindlimb motoneurons during fictive locomotion in the thalamic cat. *Experimental Brain Research* 64: 217-224, 1986.

Pang MYC, Yang JF. The initiation of the swing phase in human infant stepping: importance of hip position and leg loading. *Journal of Physiology* 528: 389-404, 2000.

Pang MYC, Yang JF. Interlimb co-ordination in human infant stepping. *Journal of Physiology* 533: 617-625, 2001.

Pearson KG. Proprioceptive regulation of locomotion. *Current Opinion in Neurobiology* 5: 786-791, 1995.

Pearson KG. Neural adaptation in the generation of rhythmic behavior. *Annual Review in Physiology* 62: 723-753, 2000.

Pearson KG, Collins DF. Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *Journal of Neurophysiology* 70: 1009-1017, 1993.

Pearson KG, Fouad K, Misiaszek JE. Adaptive changes in motor activity associated with functional recovery following muscle denervation in walking cats. *Journal of Neurophysiology* 82: 370-381, 1999.

Pearson KG, Misiaszek JE. Use-dependent gain change in the reflex contribution to extensor activity in walking cats. *Brain Research* 883: 131-134, 2000.

Pearson KG, Ramirez JM, Jiang W. Entrainment of the locomotor rhythm by group Ib afferents from ankle extensor muscles in spinal cats. *Experimental Brain Research* 90: 557-566, 1992.

Peiper A. *Cerebral Function in Infancy and Childhood*. New York, NY: Consultants Bureau, 1963.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Perret C. Centrally generated pattern of motoneuron activity during locomotion in the cat. *Symposia of the Society for Experimental Biology* 37: 405-422, 1983.

Perret C, Cabelguen J-M. Main characteristics of the hindlimb locomotor cycle in the decorticate cat with special reference to bifunctional muscles. *Brain Research* 187: 333-352, 1980.

Prochazka A, Wand P. Tendon organ discharge during voluntary movements in cats. *Journal of Physiology* 303: 385-390, 1980.

Prokop T, Berger W, Zijlstra W, Dietz V. Adaptational and learning processes during human split-belt locomotion: interaction between central mechanisms and afferent input. *Experimental Brain Research* 106: 449-456, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Rand MK, Wunderlich DA, Martin PE, Stelmach GE, Bloedel JR. Adaptive changes in responses to repeated locomotor perturbations in cerebellar patients. *Experimental Brain Research* 122: 31-43, 1998.

Roby-Brami A, Bussel B. Long latency spinal reflex in man after flexor reflex afferent stimulation. *Brain* 110: 707-725, 1987.

Rorke LB, Riggs HE. *Myelination of the Brain in the Newborn*. Philadelphia, PA: J. B. Lippincott Co., 1969.

Rossignol S. Neural control of stereotypic limb movements. In: *Handbook of Physiology, Section 12: Exercise : Regulation and Integration of Multiple Systems*, edited by LB Rowell and JT Shepherd. New York, NY: American Physiological Society by Oxford University Press, 1996, pp. 173-216.

Rowlandson PH, Stephens JA. Maturation of cutaneous reflex responses recorded in the lower limb in man. *Developmental Medicine and Child Neurology* 27: 425-433, 1985.

Sarnat HB. Do the corticospinal and corticobulbar tracts mediate functions in the human newborn? *Canadian Journal of Neurological Sciences* 16: 157-160, 1989.

Selverston AI, Panchin YV, Arshavsky YI, Orlovsky GN. Shared features of invertebrate central pattern generators. In: *Neurons Networks and Motor Behavior*, edited by PSG Stein, S Grillner, AI Selverston, and DG Stuart. Cambridge, MA: MIT Press, 1997, pp. 105-117.

Sherrington CS. *The integrative action of the nervous system.* New Haven, CT: Yale University Press, 1906.

Sherrington CS. Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. *Journal of Physiology* 40: 28-121, 1910a.

Sherrington CS. Remarks on the reflex mechanisms of the step. *Brain* 33: 1-25, 1910b.

Sinkjaer T, Andersen JB, Ladouceur M, Christensen LOD, Nielsen JB. Major role for sensory feedback in soleus EMG activity in the stance phase of walking in man. *Journal of Physiology* 523: 817-827, 2000.

Smith JL, Chung SH, Zernicke RF. Gait-related motor patterns and hindlimb kinetics for the cat trot and gallop. *Experimental Brain Research* 94: 308-322, 1993.

Smith JL, Carlson-Kuhta P, Trank TV. Forms of forward quadrupedal locomotion. III. A comparison of posture hindlimb kinematics and motor patterns for downslope and level walking. *Journal of Neurophysiology* 79: 1702-1716, 1998.

Soffe SR. Two distinct rhythmic motor patterns are driven by common premotor and motor neurons in a simple vertebrate spinal cord. *Journal of Neuroscience* 13: 4456-4469, 1993.

Stein PSG, Smith JL. Neural and biomechanical control strategies for different forms of vertebrate hindlimb motor tasks. In: *Neurons Networks and Motor Behavior*, edited by PSG Stein, S Grillner, AI Selverston, and DG Stuart. Cambridge, MA: MIT Press, 1997, pp. 61-73.

Stein PSG, McCullough ML, Currie SN. Reconstruction of flexorextensor alternation during fictive rostral scratching by two-site stimulation in the spinal turtle with a transverse spinal hemisection. *Journal of Neuroscience* 18: 467-479, 1998.

Stein RB, Misiaszek JE, Pearson KG. Functional role of muscle reflexes for force generation in the decerebrate walking cat. *Journal of Physiology* 525: 781-791, 2000.

Stephens MJ, Yang JF. Loading during the stance phase of walking in humans increases the extensor EMG amplitude but does not change the duration of the step cycle. *Experimental Brain Research* 124: 363-370, 1999.

Thach WT. A role for the cerebellum in learning movement coordination. *Neurobiology of Learning and Memory* 70: 177-188, 1998.

Thorstensson A, Roberthson H. Adaptations to changing speed in human locomotion: speed of transition between walking and running. *Acta Physiological Scandinavica* 131: 211-214, 1987.

Trank TV, Chen C, Smith JL.Forms of forward quadrupedal locomotion. I. A comparison of posture hindlimb kinematics and motor patterns for normal and crouched walking. *Journal of Neurophysiology* 76: 2316-2326, 1996.

Vecchierini-Blineau MF, Guiheneuc P. Excitability of the monosynaptic reflex pathway in the child from birth to four years of age. *Journal of Neurology, Neurosurgery, and Psychiatry* 44: 309-314, 1981.

Weber KD, Fletcher WA, Gordon CR, Jones MG, Block EW. Motor learning in the "podokinetic" system and its role during spatial orientation during locomotion. *Experimental Brain Research* 120: 377-385, 1998.

Wernig A, Müller S. Laufband locomotion with body weight support improved walking in persons with severe spinal cord injuries. *Paraplegia* 30: 229-238, 1992

Whelan PJ, Hiebert GW, Pearson KG. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Experimental Brain Research* 103: 20-30, 1995a.

Whelan PJ, Hiebert GW, Pearson KG. Plasticity of the extensor group I pathway controlling the stance to swing transition in the cat. *Journal of Neurophysiology* 74: 2782-2787, 1995b.

Whelan PJ, Pearson KG. Plasticity in reflex pathways controlling stepping in the cat. *Journal of Neurophysiology* 78: 1643-1650, 1997.

Yakovlev PI, Lecours A-R. The myelogenetic cycles of regional maturation of the brain. In: *Regional Development of the Brain in Early Life*, edited by A Minkowski. Oxford, UK: Blackwell, 1967, pp. 3-70.

Yanagihara D, Kondo I. Nitric oxide plays a key role in adaptive control of locomotion in cat. *Proceedings of the National Academy of Science USA* 93: 13292-13297, 1996.

Yanagihara D, Udo M, Kondo I, Yoshida T. A new learning paradigm: adaptive changes in interlimb coordination during perturbed locomotion in decerebrate cats. *Neuroscience Research* 18: 241-244, 1993.

Yanagihara D, Udo M. Climbing fiber response in cerebellar vermal Purkinje cells during perturbed locomotion in decerebrate cats. *Neuroscience Research* 19: 245-248, 1994.

Yang JF, Fung J, Edamura M, Blunt R, Stein RB, Barbeau H. H-reflex modulation during walking in spastic paretic subjects. *Canadian Journal of Neurological Sciences* 18: 443-452, 1991.

Yang JF, Stephens MJ, Vishram R. Infant stepping: a method to study the sensory control of human walking. *Journal of Physiology* 507: 927-937, 1998a.

Yang JF, Stephens MJ, Vishram R. Transient disturbances to one limb produce coordinated, bilateral responses during infant stepping. *Journal of Neurophysiology* 79: 2329-2337, 1998b.

Zehr EP, Stein RB. What functions do reflexes serve during human locomotion? *Progress in Neurobiology* 58: 185-205, 1999.

Zelazo PR. "Walking" in the newborn. *Science* 176: 314-315, 1972.

CHAPTER 2

COULD DIFFERENT DIRECTIONS OF HUMAN INFANT STEPPING BE CONTROLLED BY THE SAME CENTRAL PATTERN GENERATOR?

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2.1 Introduction

An important concept emerging from the study of neural networks is the idea that different motor patterns can be produced by the same circuitry given the appropriate modulatory mechanism (Marder and Calabrese 1996). These modulatory mechanisms can be a neuromodulator, afferent input, or supraspinal input (Getting 1989). Invertebrate preparations have supplied the most direct evidence for this idea (Marder and Calabrese 1996). The evidence that a single neural network produces several variants of a task is less direct in vertebrate preparations. One example of this was demonstrated during fictive swimming in the lamprey. Varying the concentration of the excitatory amino acid NMDA (N-methyl-D-aspartate) applied to different portions of the lamprey spinal cord produces changes in the intersegmental coordination (Matsushima and Grillner 1992a). If rostral segments of the lamprey spinal cord are perfused with a higher concentration of NMDA compared to the caudal segments, the fictive swimming resembles forward swimming. If the caudal portions are provided with the higher NMDA concentration, this fictive swimming reverses to the backward direction. Other neuromodulators (serotonin and GABA) can also have a role in the modulation of intersegmental coordination and burst frequency (Matsushima and Grillner 1992b; Tegnér et al. 1993).

The scratch reflex in the turtle has also provided evidence for a common neural network mediating the different forms of a task (Mortin et al. 1985; Robertson et al. 1985; reviewed in Stein et al. 1986). The three basic forms of the scratch reflex are differentially elicited by stimulation of different areas of skin (receptive fields). Blends of the forms of the reflex can also be elicited by stimulation of transitional zones that are situated between receptive fields. These blended responses show characteristics of scratch responses elicited from both adjacent receptive fields. In addition, the segments of the turtle spinal cord which are required for the different forms of the scratch response have been identified and shown to be localized within the same region (spanning four spinal cord segments) (Mortin and Stein 1989). Moreover, there is compelling evidence that the neural circuitry for one form of the scratch reflex is shared with the circuitry for the other forms of the scratch reflex (Stein et al. 1998). These findings in the turtle are consistent with the idea that there are common neural network components that control the different forms of the scratch response.

In mammals, the idea of a common neural network underlying different forms of a behaviour has been supported in studies of different forms of cat locomotion. The evidence, however, is far less conclusive than that from invertebrate and simple vertebrate preparations. Intact cats can modify their locomotor pattern to produce speed-related changes (i.e. walk, trot, gallop) (Smith et al. 1993), upslope and downslope walking (Smith and Carlson-Kuhta 1995; Carlson-Kuhta et al. 1998; Smith et al. 1998a), crouched walking (Trank et al. 1996), and backward walking (Buford and Smith 1990). The ability of cats to alter their locomotor patterns in this way could be explained by reconfigurations in the locomotor CPG model originally proposed by Grillner (1981) (Smith et al. 1998b). These central reconfigurations may be accomplished by supraspinal input (Stein and Smith 1997).

Stein et al. (1986) observed that humans are also able to continuously change their direction of stepping in a smooth and automatic manner. Are the different forms of walking controlled by the same circuitry? Thus far, forward and backward walking have been studied in adult humans. A consistent result from these studies is the almost perfect reversal in the joint kinematic profile when comparing backward to forward walking (Thorstensson 1986; Vilensky et al. 1987; Winter et al. 1989; Grasso et al. 1998). In contrast, muscle activation patterns are more varied. Results among different laboratories show neither a consistent preservation nor a strict reversal in coupling of muscles between the forward and backward direction (Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). Grasso et al. (1998) suggested that the preservation of kinematic profiles occurs at the expense of muscle activation patterns, but their results neither support nor refute the possibility that a common neural network is producing the different forms of walking.

Studying adult human walking, however, is not the ideal approach to determine the ability of the human locomotor central pattern generator (CPG) to produce different forms of locomotion. Higher brain centres can intervene at any time and their contribution cannot be distinguished from that originating from the brainstem/spinal circuitry. Recently, human infants were introduced as an alternative model for studying CPG control of locomotion in humans (Yang et al. 1998a).

Infants exhibit a stepping response that is thought to be mostly under the control of spinal and brainstem circuitry (Peiper 1963; Forssberg 1985). Indirect evidence from a number of sources suggests that the strength of connections from the motor cortex is weak in infants. For example, the threshold for eliciting muscle activity in the upper limbs using transcranial magnetic stimulation over the motor cortex is extremely high in young children under 2 years of age (Koh and Eyre 1988; Eyre et al. 1991; Müller et al. 1991). When it is possible to elicit responses, the conduction velocities are more than an order of magnitude slower than adults in infants under the age of 1 (Koh and Eyre 1988). Histologically, the corticospinal tract is not fully myelinated until the age of 2 (Yakovlev and Lecours 1967).

Behaviourally, children do not use the fingertip and thumb in opposition to grasp objects (pincer grip) until 6 months of age at the earliest (Halverson 1943). Development of the pincer grip in monkeys was correlated with the maturation of the corticospinal tract to the cervical enlargement; this occurs around the age of 7 months (Hall et al. 1992; Flament et al. 1992b). Maturation of connections to the lumbar enlargement occurs shortly thereafter (Flament et al. 1992a). Thus, with the current information, it is reasonable to suggest that infant stepping is not likely under strong cortical control. We cannot rule out the possibility that indirect pathways from the cortex are mature in the infant. Nevertheless, while it is important that we continue to seek evidence for the state of maturation of motor tracts in infants, we believe infants provide a unique opportunity to study the neural control of locomotion before extensive influence from the cerebrum is present.

The goal of this study was to determine whether different directions of stepping in human infants might be produced by one central pattern generator system. We reasoned that if the same circuitry can produce all directions of stepping, then i) infants who can step in one direction will be able to step in all other directions; ii) infants will respond in the same way to speed changes regardless of the direction of stepping; and iii) changes in direction of stepping can be achieved in a continuous manner without any discontinuity in the stepping rhythm. The incidence of stepping across different age groups, temporal parameters of gait, and the continuous manner in which infants altered their stepping direction provided evidence supporting the idea that different directions of locomotion can indeed be mediated by a common neural network. Preliminary results have been published in abstract form (Yang et al. 1998b).

2.2 Methods

2.2.1 *Subjects and Preparation*

Fifty-two infants (male and female) ranging in age from 2 months to 11 months were studied. Infants were recruited from the maternity ward of a local hospital and from some local community health clinics. Parents were required to give voluntary and written consent on behalf of their infant for participation in the study. Ethical approval was obtained from the University of Alberta and the local health authority.

Recording electrodes (silver-silver chloride surface electrodes, Beckman type) were placed on the skin overlying the tibialis anterior (TA), gastrocnemius/soleus (GS), quadriceps (Quad), and hamstrings (Hams) muscles after cleaning the skin with rubbing alcohol. In most infants, electromyographic (EMG) recordings were taken from one side. In the other infants, EMG recordings were taken from only the GS and TA muscles from both legs. Regular-sized electrodes (7 mm recording diameter) were used unless the infant was very young or very small, in which case miniature electrodes (2 mm recording diameter) were used. The electrode pairs were separated by 1 to 2 cm. Force sensitive resistors (FSRs) (Interlink Electronics, Camarillo, CA) were taped to the soles of the feet to record the time of contact each foot makes with the treadmill surface. Adhesive joint markers were placed over the superior border of the iliac crest, the greater trochanter of the femur, the knee joint line, the lateral malleolus, and the head of the fifth metatarsal on both legs. In some infants, joint markers were also placed over the anterior aspect of the ankle joint, over the superior border of the patella, directly under the anterior superior iliac spine (ASIS) and on the abdomen directly above the ASIS to obtain limb segment motion data from a coronal view for sideways stepping. Skin markers will, of course, move with the skin, so they cannot indicate the precise position of a segment. We are interested in the gross movements of the limbs during stepping, for which these markers are adequate. The analog data from the electrodes and FSRs were recorded on VHS tape with a pulse-code modulated encoder (A.R. Vetter Co. Inc., Rebersburg, PA). A video camera was used to record the motion from one side. A digital timer synchronized the analog and video data by generating a light signal on video and a pulse on analog tape at a rate of 1 Hz.

To elicit stepping, infants were held under their arms with their feet touching a slowly moving treadmill belt (0.1 to 0.6 m/s). The infant was allowed to bear as much of his or her own weight as possible, the rest being supported by the investigator holding the infant. Short trials (0.5 to 2 minutes, depending on the infant's endurance) were recorded with rest breaks in between.

If an infant could step forward, he or she was then tested in the other directions of stepping. Infants who did not show forward stepping were excluded from the study. Backward stepping was defined as those steps in which the infant's leg actively moved backward so that the lateral malleolus reached a point posterior to the greater trochanter. Sideways stepping was defined as those steps in which the leading leg was observed to be abducting and the trailing leg adducting past neutral. The infant was held facing different directions with respect to the motion of the treadmill belt in order to achieve stepping in these directions. Additionally, attempts were made in some infants to gradually turn them along a 180º path during stepping to achieve a continuous sequence of stepping in all directions. For some infants, different directions of stepping were elicited at a range of speeds. Stepping sequences must have comprised at least 4 consecutive steps to be accepted for further analysis.

2.2.2 Data Analysis

Video data was examined for sequences of sustained, alternating stepping. The EMG data were high-pass filtered at 10 Hz, low-pass filtered at 30 Hz, and full-wave rectified. All the analog data from the EMGs, the FSRs, and synchronization light were converted to digital form at 200 Hz using a computer software program (Axoscope, Axon Instruments Inc., Foster City, CA). EMG and FSR data were averaged over single cycles with alignment to the beginning of foot contact, as indicated by the FSRs or video image. Data were analyzed separately according to the direction of stepping. All stepping sequences occurring in a particular direction at a given speed were averaged together. Only noise-free EMG data were included in the averages. The averaged EMG recordings from backward and sideways stepping were normalized to the peak EMG for each muscle obtained from the forward stepping trials at the same speed. These averaged EMG traces over a step cycle were then normalized in time by distributing the trace into a series of 100 time sections using a custom-written computer program (MATLAB, MathWorks, Natick, MA).

Co-contraction was calculated in a similar manner as reported in a previous paper (Yang et al. 1998a). The area under averaged and normalized noise-free EMG data from the TA and GS muscle groups was calculated after removing a bias using a custom-written computer program (MATLAB, MathWorks, Natick, MA). The bias was defined as a 50-100 ms period of quiescent muscle activity within the averaged and normalized data. The area under the averaged EMG from a muscle was defined as 100%, and the amplitude at each point in time expressed as a percentage of this total. The index of co-contraction was defined as the overlap in area between the TA and GS muscles. For example, if at a given point in time in the step cycle both EMGs were not zero, then the overlap at that time was given as the EMG with the lower amplitude. The total index of co-contraction in the step cycle is the sum of these individual overlap points with the maximum possible overlap being 100%. Indices were calculated for forward, backward, and sideways stepping. The co-contraction indices were compared with data obtained from a previous study (Yang et al. 1998a) using Student's *t*-test. The co-contraction indices were also compared between forward, sideways, and backward stepping using ANOVA.

The success in eliciting backward and sideways stepping was compared across age groups. The incidence of backward and sideways stepping was expressed as a percentage of infants who could step forward.

A repeated measures analysis of covariance (ANCOVA), with speed as the covariate, was used to determine differences in stepping frequency between forward, backward, and sideways stepping (leading leg and trailing leg). Stepping frequency was defined as the reciprocal value of cycle duration, also called cadence. Since individual infants stepped best at different treadmill speeds, the effect of speed on stepping frequency could be factored out. Cycle duration of infant stepping is not linearly related to treadmill speed (Yang et al. 1998a). Thus, stepping frequency (the reciprocal value of cycle duration) was used as the dependent measure since it has a linear relationship to speed, thus conforming with the assumptions of the ANCOVA model (Glass and Hopkins 1996). In addition, only data where an infant walked at the same treadmill speed for the three directions were used for the ANCOVA.

The relationship between stance and swing (phase) duration and cycle duration was described with a linear regression line. To test whether the relationship between phase duration and cycle duration was significantly different between the different directions of stepping, the Welch t' test was used to compare the slope (regression coefficient, *b*) values between each direction, using data from forward stepping as the reference (Pedhazur 1982; Glass and Hopkins 1996). Significance was evaluated at a level of 0.05 for all of the above statistical tests.

To quantify differences in muscle activity patterns between the different directions of stepping, a repeated measures analysis of variance (ANOVA) was used to compare average EMG amplitude. Data from an individual infant was included only if the infant contributed data to forwards stepping and at least one other direction (i.e. backwards or sideways). Of the total 52 infants tested, 34 were tested for both backward and sideways stepping. Each cycle of normalized and averaged EMG recording for each muscle was divided into 10 equal bins (i.e. representing one-tenth of the step cycle) and the average EMG amplitude within each of these bins was calculated. The division of the step cycle into ten bins is arbitrary. It was chosen to allow estimates of the stance and swing phases (bins 1 to 6 roughly correspond to the stance phase and bins 7 and 10 correspond to the swing phase). We felt this was the most appropriate way to divide the step cycle without making the statistical tests too cumbersome. The following comparisons on EMG amplitude were conducted: forward vs. backward, forward vs. the leading leg of sideways, and forward vs. the trailing leg of sideways. The Dunn (Bonferroni) method of multiple comparisons was used to compare the data post hoc. Thus, the level of significance was adjusted to 0.005 to account for the 10 post-hoc comparisons to minimize the increase in type I errors associated with multiple comparisons (Glass and Hopkins 1996).

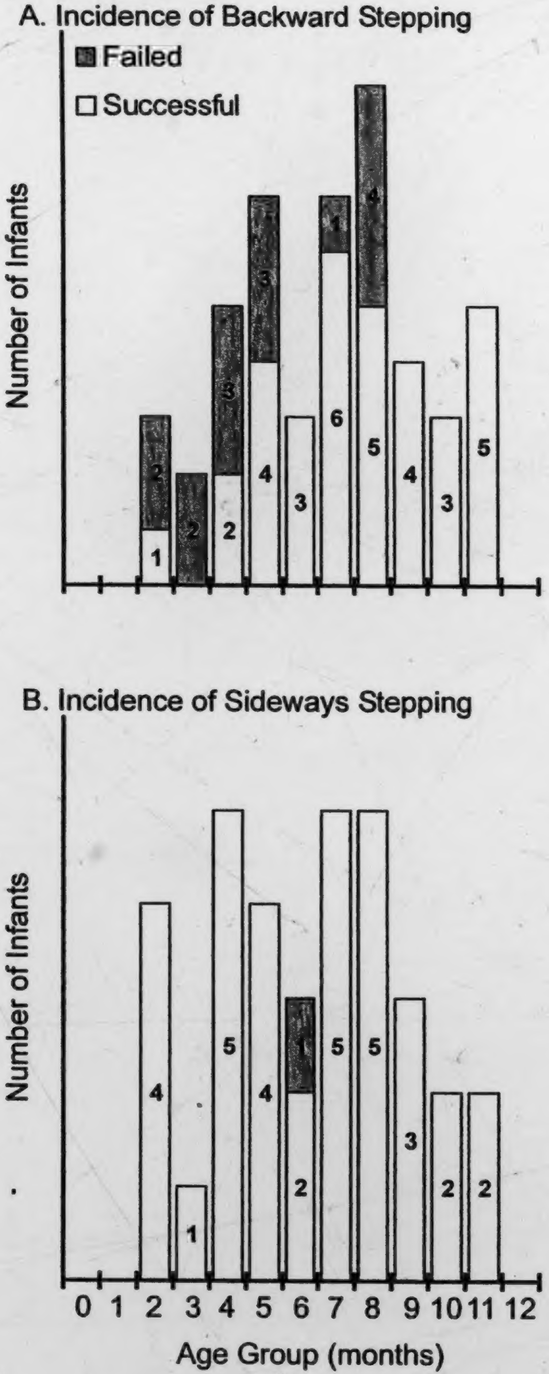
2.3 Results

2.3.1 Incidence of Stepping in Different Directions

Backward stepping was attempted in 48 of the 52 infants. Thirty-three infants successfully demonstrated sustained, alternating stepping in a backward direction (69% success rate). Backward stepping could be elicited in an infant as young as 2 months old. By 9 months old, all infants tested could step backward consistently (Fig. 2.1). Sideways stepping was attempted in 34 infants. All except one were successful in demonstrating sustained, alternating sideways stepping (97% success rate). Interestingly, sideways stepping appears to be more easily elicited than backward stepping, especially when comparing infants in the younger age groups (2 to 5 months) (Fig. 2.1). However, it is important to note that of the infants who "failed" the backward stepping criteria (n = 15), only 3 (aged 2 to 3 months) showed no response at all. In the remaining 12 infants, alternating stepping movements were elicited, but the stepping did not meet our criteria for backward stepping. In most of these infants, the stepping movements resembled in-place stepping, rather than backward stepping. In 3 of the 12 infants (all in the 8 month age group), backward stepping by a single limb was observed. In these cases, the recording limb was held stiff while the other limb made backward stepping movements. Other than the fact that these steps were not alternating, these infants met our backward stepping criteria. We presume that the presence of the electrodes and joint markers on the recording limb produced peculiar sensory inputs that might have interfered with the infants' stepping patterns.

Figure 2.1. Incidence of Backward and Sideways Stepping.

Incidence of stepping in (*A*) backward and (*B*) sideways directions in infants who could step forward. The numbers inside the bars represent the number of infants in each group.



A. Incidence of Backward Stepping

B. Incidence of Sideways Stepping

Figure 2.2A shows stick figures of forward and backward stepping from a 9-month-old infant. In contrast to forward and backward walking in adults (Thorstensson 1986; Vilensky et al. 1987; Winter et al. 1989; Grasso et al. 1998), the kinematic profiles do not show a symmetrical reversal in time. This infant's averaged EMG traces are shown later (Fig. 2.6). Figure 2.2*B* shows stick figures taken from a 5-month-old infant stepping forward, sideways, and backward. This infant was also one who did not meet our backward stepping criteria (note that the ankle joint is never positioned posterior to the hip joint). However, stepping movements did occur. When comparing the infants in figures 2.2A and 2.2B, it is clear that the younger infant was more flexed during forward stepping. During backward stepping, the younger infant was not able to extend the hip beyond neutral. This is typical of many of the infants who failed our backward stepping criteria. This flexed posture may account for the inability of many of the younger infants to meet our backward stepping criteria since the legs are at a biomechanical disadvantage to extend backward.

2.3.2 Temporal Parameters of Stepping in Different Directions

Figure 2.3A demonstrates the strong linear correlation between stepping frequency and treadmill speed ($p < 0.01$ for each direction of stepping). The ANCOVA ($n = 26$) yielded no significant difference in stepping frequency between the different directions of stepping. However, it does appear that there was a general trend of increasing stepping frequency (i.e. decreasing cycle duration) from forward to sideways to backward stepping (Fig. 2.3*B*).

Much of the change in cycle duration with speed was due to the change in stance duration for forward ($r^2 = 0.92$), backward ($r^2 = 0.94$), and sideways (leading leg) stepping

Figure 2.2. Kinematic Figure of Forward, Backward, and Sideways Stepping.

A. Stick figures from a 9-month old infant stepping forward and backward. The step starts from the stick figure at the far right (initial foot contact). The inter-frame interval is 33 ms. Both illustrations show limb segment motion over two successive step cycles. Each successive stick figure is shifted to the left for clarity. The thick black line delineates the swing phase. *B*. Stick figures from a 5-month old infant stepping forward, sideways (trailing leg), and backward. The convention is the same as that for A. In this case, only one step cycle is illustrated. Sideways stepping is diagrammed from the coronal view. In this example, the trailing leg collides with the leading leg causing a prolongation of the swing phase. The apparent change in ankle angle during sideways stepping is due to out-of-plane rotation at the ankle that occurred during the step cycle. The backward stepping illustrated here is an example of one that did not meet our criteria (see text).

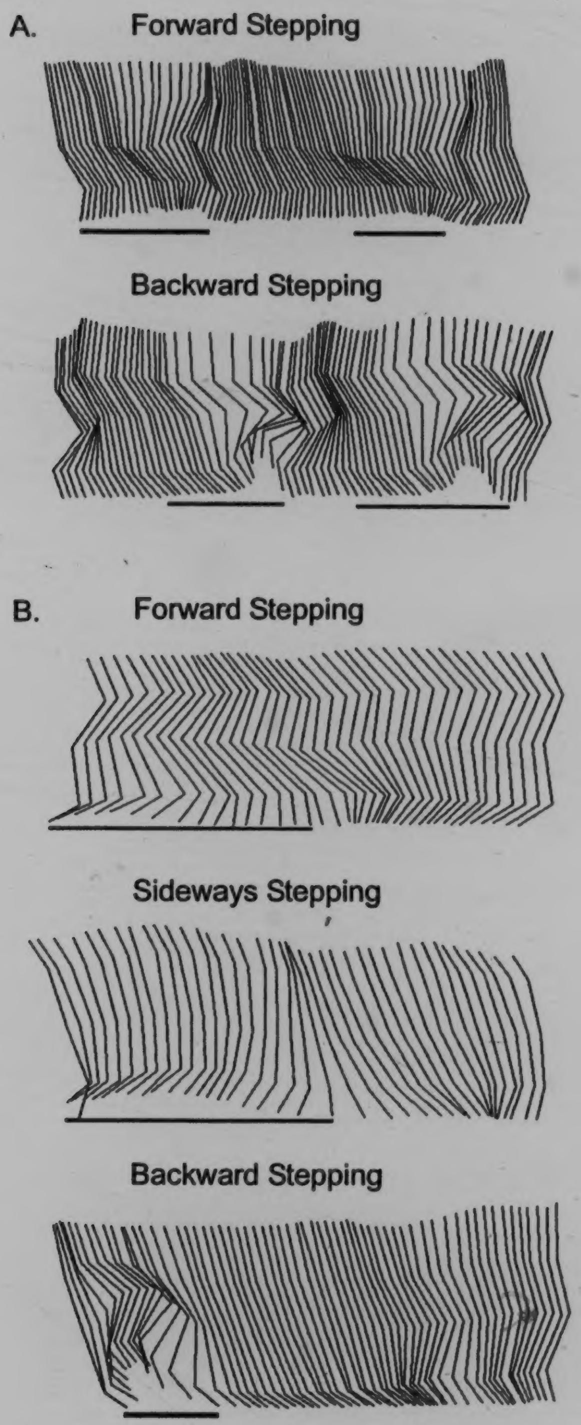
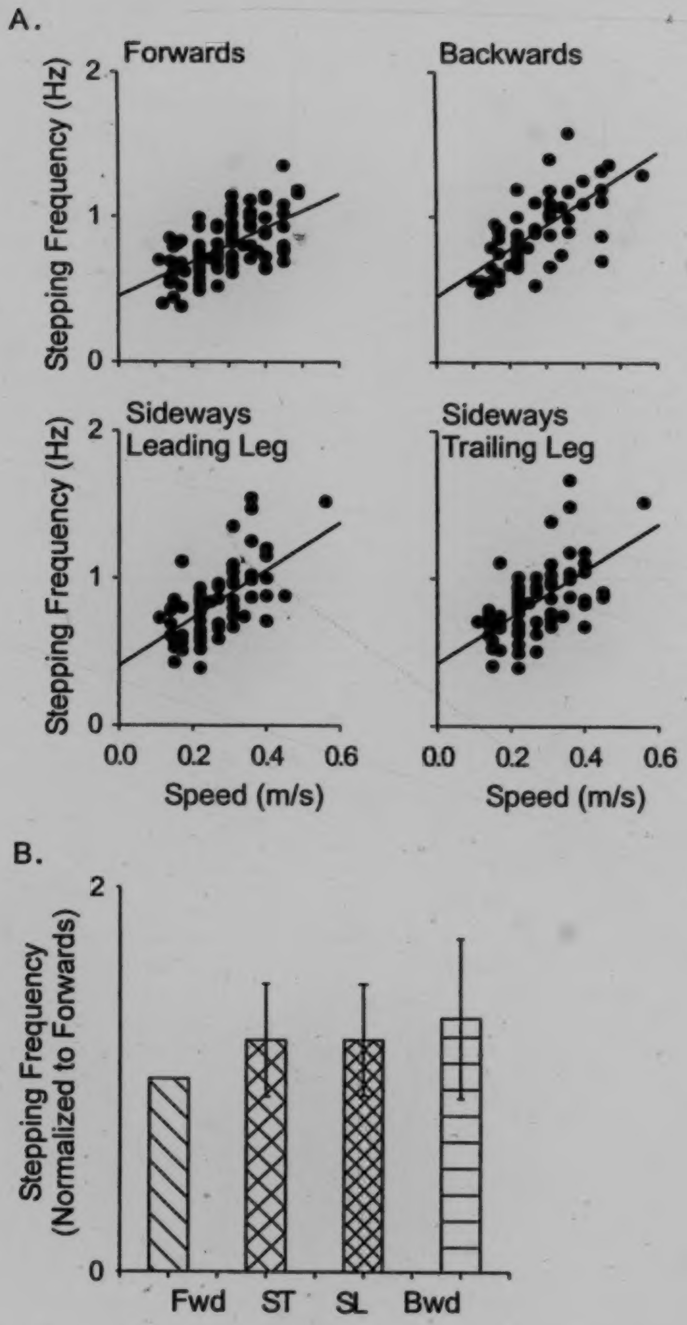

A.
Forward Stepping
Backward Stepping
B.
Forward Stepping
Sideways Stepping
Backward Stepping

Figure 2.3. The Response to Changes in Treadmill Speed.

A. Stepping Frequency (Hz) vs. Treadmill Speed (m/s). For all directions of stepping, there is a strong linear correlation between stepping frequency and treadmill speed. Pearson product-moment correlation (r) values are as follows: 0.62 for forward, 0.69 for backward, 0.62 for the leading leg of sideways, 0.59 for the trailing leg of sideways. All r values are significant ($p < 0.01$). *B.* Stepping Frequency Normalized to Forwards vs. Direction of Stepping. Only the data from infants who stepped in all 3 directions at a given speed were included. A general trend of decreasing cycle duration as stepping direction changes from forward to sideways to backward is clear. The error bars represent standard deviation.


A.
Forwards
Backwards
Sideways Leading Leg
Sideways Trailing Leg
Stepping Frequency (Hz)
Stepping Frequency (Hz)
0
1
2
0.0
0.2
0.4
0.6
Speed (m/s)
Speed (m/s)
B.
Stepping Frequency (Normalized to Forwards)
0
2
Fwd
ST
SL
Bwd

($r^2 = 0.89$) (Fig. 2.4). Swing duration was more weakly related to cycle duration for these same directions of stepping (r^2 values range from 0.33 to 0.64). In the trailing leg of sideways stepping, there was a different relationship between phase and cycle duration. In this case, both the stance and swing durations varied with cycle duration (r^2 values of 0.49 and 0.70, respectively). For the relationship between phase (stance and swing) and cycle duration, there was no significant difference in the slope (b) values between forward and backward, and forward and the leading leg of sideways stepping. In contrast, the trailing leg in sideways stepping differed significantly from forward stepping ($p = 0.0016$ for stance; $p = 0.0008$ for swing).

2.3.3 EMG Patterns

Figure 2.5 illustrates the index of co-contraction averaged across all subjects who showed good EMG recordings from the TA and GS muscles. Yang et al. (1998a) previously showed that the co-contraction index for the TA-GS pair was significantly higher in infants compared to adults. In the present set of data, we found no significant difference in the co-contraction index for any direction of stepping with that reported previously for infants (Yang et al. 1998a). In addition, there was no significant difference between co-contraction indices between the different directions of stepping.

An example of TA-GS co-contraction is seen in figure 2.6. This figure illustrates the averaged EMG pattern of step cycles from a single representative subject stepping in three different directions at the same speed. Note the activity in the TA muscle, corresponding to activity in the GS muscles during stance phase. Indeed, the co-contraction indices from the

Figure 2.4. Phase Duration vs. Cycle Duration.

Each data point represents the average duration over the number of steps taken from an infant at a given treadmill speed. Error bars represent one standard deviation of each of these sets of data. For forward (*A*), backward (*B*), and sideways (leading leg) (*C*) walking, stance duration accounted for much of the response to speed change. Stance duration is much more highly correlated with cycle duration than swing duration. However, for the trailing leg in sideways stepping (*D*), stance and swing duration seem to be equally correlated with cycle duration. The slope of the relationship between phase duration and cycle duration is represented by *b*.

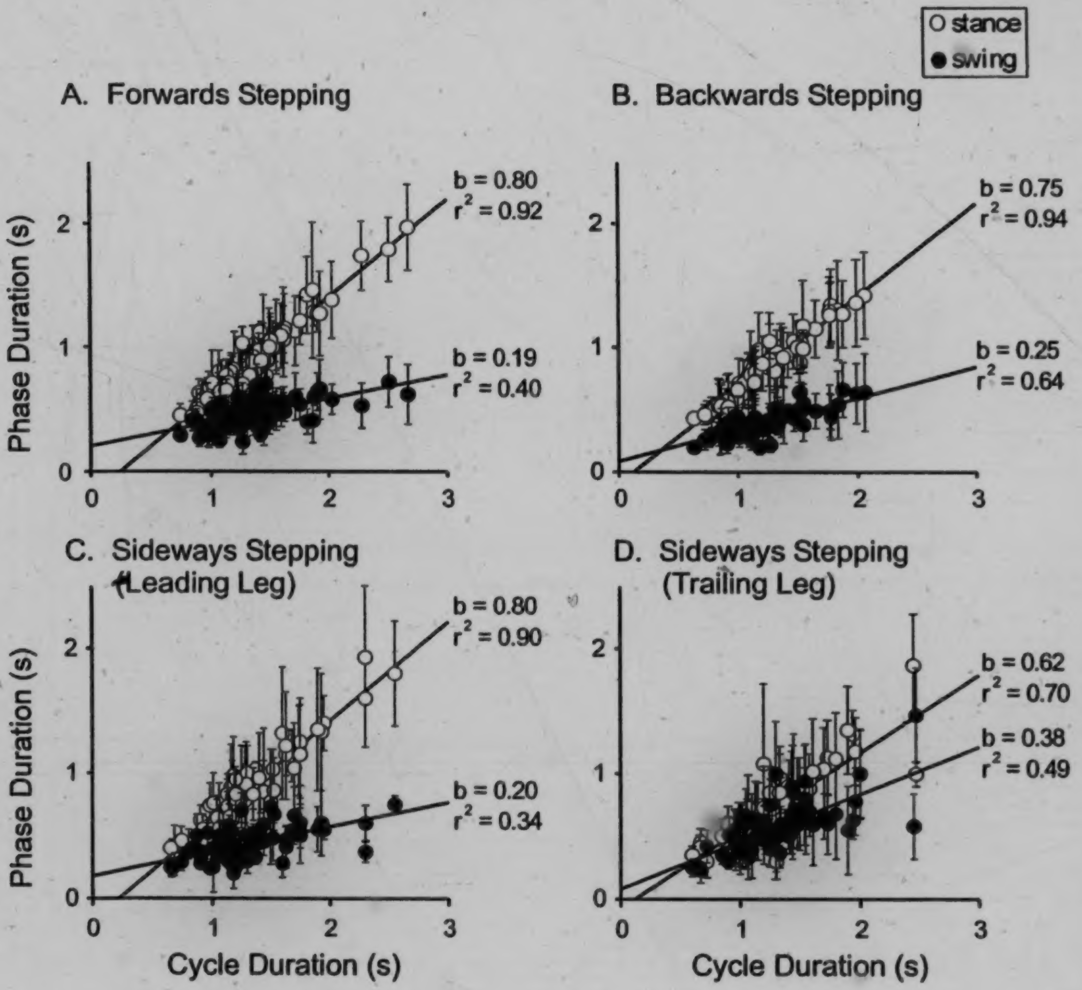

○ stance
● swing
A. Forwards Stepping
B. Backwards Stepping
C. Sideways Stepping (Leading Leg)
D. Sideways Stepping (Trailing Leg)
Phase Duration (s)
Cycle Duration (s)
0
1
2
3
b = 0.80
$r^2 = 0.92$
b = 0.19
$r^2 = 0.40$
b = 0.75
$r^2 = 0.94$
b = 0.25
$r^2 = 0.64$
b = 0.80
$r^2 = 0.90$
b = 0.20
$r^2 = 0.34$
b = 0.62
$r^2 = 0.70$
b = 0.38
$r^2 = 0.49$

Figure 2.5. Index of Co-Contraction during Forward, Backward, and Sideways Stepping.

The co-contraction index for each direction of stepping was not significantly different between the different directions and between the values reported previously by Yang et al. (1998a). The data represent pooled data from 21 infants and the error bars represent the standard deviation.

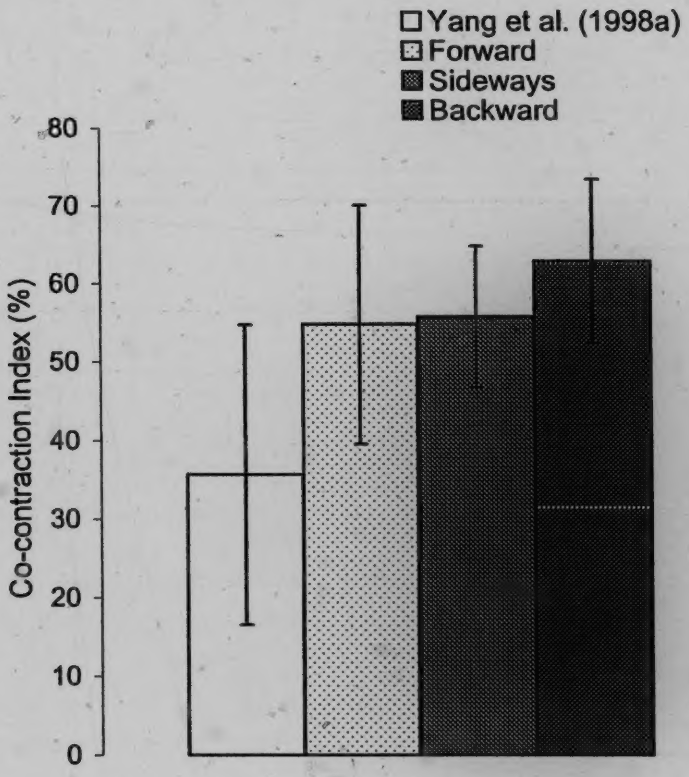
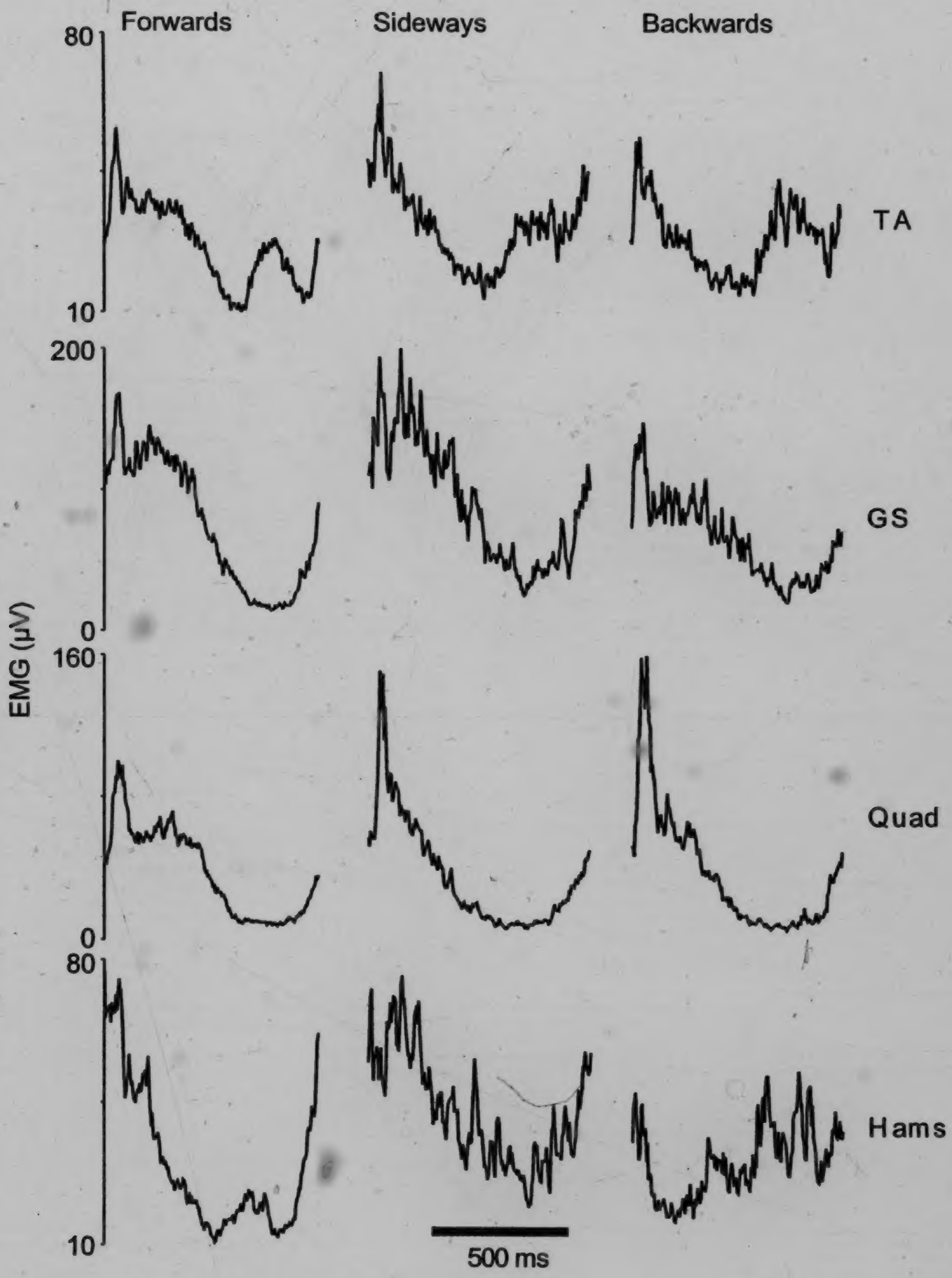

Yang et al. (1998a)
Forward
Sideways
Backward
Co-contraction Index (%)
80
70
60
50
40
30
20
10
0

Figure 2.6. Muscle Activation Patterns for Different Directions of Stepping.

Example of average rectified and filtered EMG records from stepping in each direction from a 9-month old infant. Number of steps averaged in each direction: 33 forward, 17 sideways, 15 backward. Sideways stepping was recorded from the trailing leg. Treadmill speed is 0.31 m/s. Steps are aligned to foot contact. Abbreviations: TA, tibialis anterior; GS, gastrocnemius-soleus; Quad, quadriceps; Hams, hamstrings.


Forwards
Sideways
Backwards
80
10
200
0
160
0
80
10
EMG (μV)
TA
GS
Quad
Hams
500 ms

TA-GS muscle pair calculated from this infant were higher than average (82% during forward stepping, 72% during sideways stepping, and 64% during backward stepping).

Overall, the EMG bursts from a particular muscle generally occurred at the same time in the step cycle regardless of the direction of stepping. The only exception was the hamstring muscle group in which activity started earlier in the swing phase during backward stepping. Similar trends were seen when the data were averaged across subjects (Fig. 2.7). Nine comparisons turned out to be significantly different ($p < 0.005$) (see figure legend, Fig. 2.7). The statistical tests may have been too restrictive, however, and thus unable to detect some of the obvious differences seen in figure 2.7. However, some interesting trends were noted and will be discussed below. The number of infants who contributed data to the EMG averages is shown in Table 2.1.

The EMG waveforms for forward stepping were most similar to those of the leading leg of sideways stepping. Even in this comparison, however, some differences were noted. For example, the flexor muscles (TA and Hams) were in general more active during sideways stepping than forward stepping (Fig. 2.7*B*, C). The differences between the extensor muscles were most obvious for the trailing leg in sideways stepping. Presumably, the propulsive action of extensors is not as important for the trailing leg.

The EMG was most different for the hamstring muscle between forward and backward stepping. The strong activity of the hamstrings during backward stepping was probably important for generating the hip extension and knee flexion needed during the swing phase (see Fig. 2.7A). The extensor muscles also showed some differences. The GS does not show the propulsive activity in late stance during backward stepping. This trend is

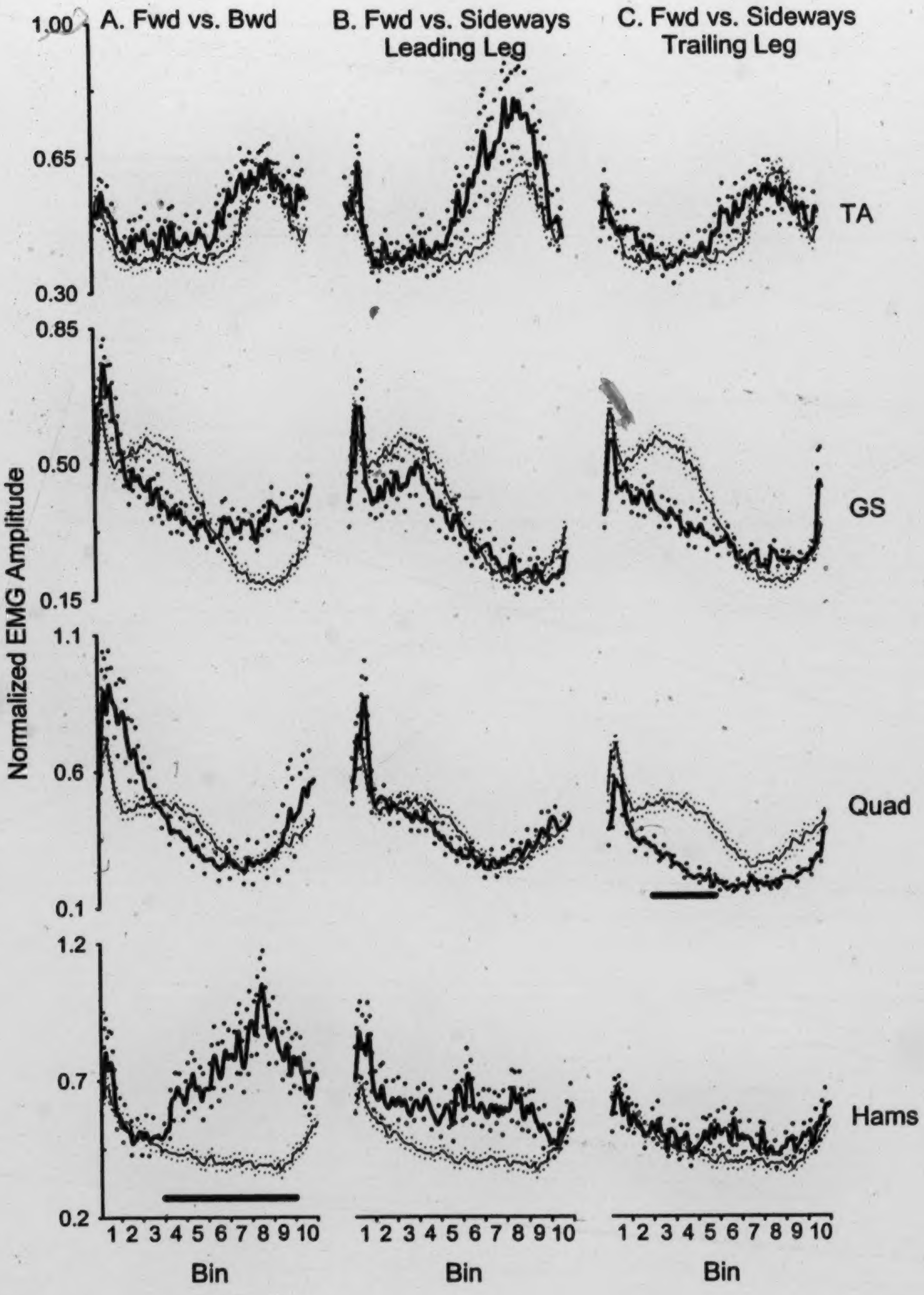
Table 2.1. Number of Infants who Contributed EMG Data.

Number of infants who contributed EMG data for each muscle in each direction of stepping. Age range: 2 to 11 months. Abbreviations: TA, tibialis anterior; GS, gastrocnemius-soleus; Quad, quadriceps; Hams, hamstrings; SL, leading leg of sideways stepping; ST, trailing leg of sideways stepping.

	TA	**GS**	**Quad**	**Hams**
Forward	24	26	22	21
Backward	17	18	14	13
SL	12	12	12	12
ST	12	12	10	9

Figure 2.7. EMG Patterns Averaged across Subjects for Different Stepping Directions.

A. Normalized EMG traces begin at the onset of foot contact. Vertical axes are constant across the three directions for each muscle. Thin lines represent averaged EMG signals from forward stepping and thick lines represent other directions of stepping. Dotted lines represent ± 1 standard error. The amplitude of the hamstrings during swing was significantly different between forward and backward stepping ($p < 0.005$, indicated by the thick bar from bin 4 through 9). Quadriceps, TA, and G-S muscles show similar activation patterns with little difference in timing and only slight (non-significant) differences in amplitude. *B.* shows forward vs. sideways (leading leg) EMG patterns and C. shows forward vs. sideways (trailing leg) EMG patterns. Only quadriceps activity during late stance is significantly different between forward and the trailing leg of sideways stepping ($p < 0.005$, indicated by the thick bar from bin 3 through 5). Abbreviations: TA, tibialis anterior; GS, gastrocnemius-soleus; Quad, quadriceps; Hams, hamstrings; Fwd, forward stepping; Bwd, backward stepping.


A. Fwd vs. Bwd
B. Fwd vs. Sideways Leading Leg
C. Fwd vs. Sideways Trailing Leg
Normalized EMG Amplitude
1.00
0.65
0.30
0.85
0.50
0.15
1.1
0.6
0.1
1.2
0.7
0.2
TA
GS
Quad
Hams
1 2 3 4 5 6 7 8 9 10
Bin

also seen in adult walking, where the quadriceps take over more of the propulsive role normally assumed by the plantarflexors (Winter et al. 1989).

2.3.4 *Transitions*

In some trials, attempts were made to gradually turn the infant continuously from a forward to sideways to backward orientation during a sequence of stepping (stepping through a 180° path). This was attempted in 14 infants ranging in age from 2 to 11 months old. Of the infants tested, 8 were able to step from the forward through sideways to the backward direction. Of these 8 infants, however, only 2 were able to make the transition through 180° in a smooth and continuous manner. The 6 other infants did show stepping in the transition directions, but were not considered to have made smooth transitions. Typically, their legs collided with each other during the transition directions, causing a disruption in their stepping. The forward to sideways transition appears to be more easily elicited than the transition into backward stepping as 11 of the 14 infants were able to step continuously from forward to sideways. In 2 of the 14 infants, smooth transitions were not made into any direction. In these infants, stepping to criteria was not elicited during the transition from one direction to another. In 4 other infants, only the forward to sideways transition was attempted. All 4 of these infants were successful in this attempt. Transitions were always attempted in the forward-sideways-backward order except in one infant where the order was reversed. Figure 2.8 shows the progressive decrease in stance phase duration in an infant who was able to make a smooth transition from forward to sideways to backward stepping. Figure 2.9 illustrates some examples of rectified and filtered EMG signals of single steps in the different directions. Generally, there was a gradual decrease in

Figure 2.8. Transitions between Different Directions: Temporal Patterns during Stepping.

Average duration of stance phase (with standard deviation) expressed as a proportion of cycle duration for each direction in a 6-month old infant who was able to make a continuous change in direction while stepping on the treadmill. There is a trend of a progressive decrease in the proportion of the cycle duration devoted to stance phase as stepping proceeds from the forward to sideways to backward direction.

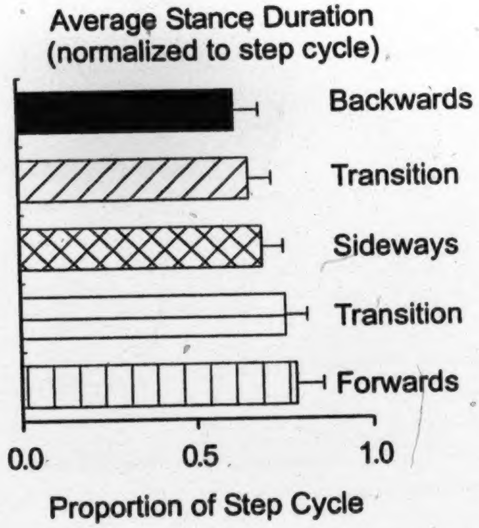
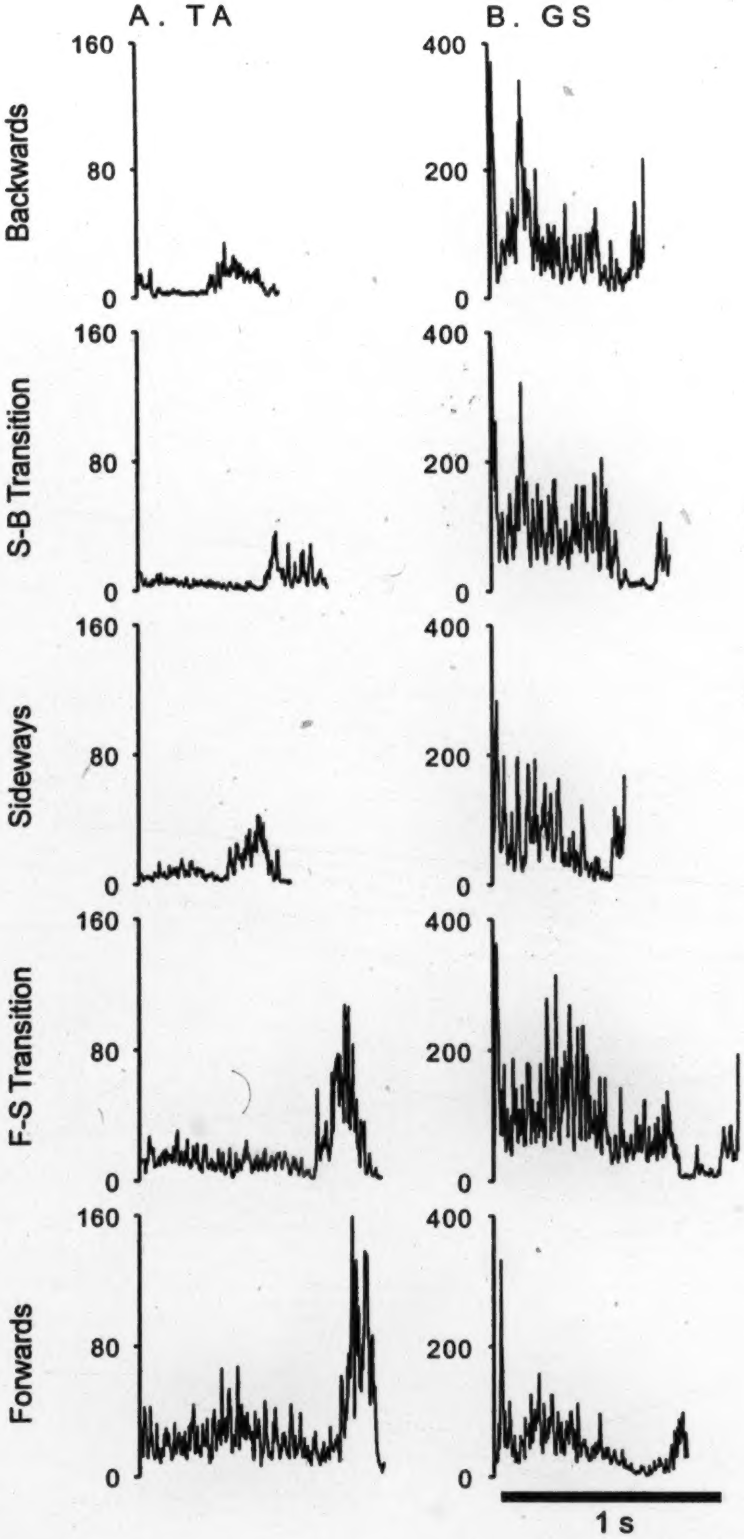

Average Stance Duration
(normalized to step cycle)
Backwards
Transition
Sideways
Transition
Forwards
0.0
0.5
1.0
Proportion of Step Cycle

Figure 2.9. Transitions between Different Directions: Muscle Activation Patterns during Stepping.

Rectified and filtered EMG signals from two infants. A. illustrates TA muscle activity from a 10-month old infant. Sideways stepping was recorded from the trailing leg. B. illustrates GS activity from a 6-month old infant. Sideways stepping was recorded from the leading leg. For each muscle, the three main directions plus the transition direction are shown. Abbreviations: F-S, forward to sideways; S-B, sideways to backward. EMG signals are illustrated in real time and units are in microvolts.


A. TA
B. GS
Backwards
S-B Transition
Sideways
F-S Transition
Forwards
160
80
0
400
200
0
1 s

cycle duration as stepping proceeds from the forward to sideways and finally to the backward direction. Both the TA and GS muscles showed a striking conservation of motor patterns across all directions of stepping (Fig. 2.9). Note that in this example, TA activity in this particular infant during forward stepping tended to be higher than other directions of stepping (cf. Fig. 2.7). Hamstrings and quadriceps EMG records are not illustrated because their EMG signals tended to be smaller and therefore less clear without averaging.

2.4 Discussion

The data show that infants are able to step in different directions at all ages tested and adapt their stepping to changes in speed in the same way regardless of the direction of stepping. Furthermore, infants can make transitions between the different directions of stepping in a continuous way. We argue that these findings are consistent with the idea that the same pattern generators for locomotion can produce different directions of stepping.

2.4.1 Methodological Considerations

There were a number (15) of young infants (4 months old and under) that were classified as "failures" for backward stepping. Nine out of 15 of these infants demonstrated alternating stepping movements when presented with a treadmill belt moving backward under their feet, but failed our criteria because of inadequate hip extension. Three other infants stepped backward very well with one leg while holding the other leg stiff, again failing our definition of stepping. In the final three infants, who were the youngest of the infants tested (aged 2 to 3 months), no backward stepping response was elicited at all. Our criteria for backward stepping were set arbitrarily, however, and may have been too stringent for young infants. The fact that 80% (12 out of 15) of these failures produced some form of stepping suggests that stepping can be produced by backward movement of the treadmill belt in the majority of infants.

EMG recordings from infants are always more likely to contain cross-talk between muscles, because of the small stature of infants. This issue is discussed at length in an earlier paper (Yang et al. 1998a) and a method was reported to estimate the degree of overlap in activity between flexors and extensors. Using the same methods, we established that the overlap between antagonistic muscles in this study was approximately the same. However, the presence of reciprocal activation of antagonist muscles demonstrates that the cross-talk, although present, is present only in a limited way (see Fig. 2.7, TA vs. GS, Quad vs. Hams). Furthermore, the comparison of patterns between muscle groups is not integral to our central thesis. Our focus is on how a particular muscle performs in different tasks. Thus, the effect of a small amount of cross-talk between muscles should not greatly compromise this comparison.

2.4.2 The Response to Speed is Similar for the Different Directions of Stepping

The response to speed change was similar for all directions of stepping tested. The similarity in the response to this type of external perturbation argues for the presence of a common locomotor network mediating stepping in different directions. Changes in cycle duration in response to speed changes were accomplished primarily by changing the stance duration, regardless of the direction of stepping. In a number of infants, we attempted to elicit continuous stepping through 180° and we observed changes of a continuous nature as stepping proceeded through the different directions. For instance, there was a progressive decrease in cycle duration as stepping proceeded from forward to sideways to backward at a given speed. Concomitant with this was the steady decrease in the proportion of cycle duration devoted to the stance duration.

In addition, the slopes of the regression lines describing the relationship between the phases of the cycle (stance and swing) and cycle duration were not statistically different between the different directions. The only difference seen was in the trailing leg of sideways stepping. However, this difference may be due to the style of sideways stepping. Most infants stepped sideways without crossing one leg over the other. This non-crossing pattern of stepping resulted in the trailing leg frequently colliding with the leading leg at the end of swing (e.g. Fig. 2.2*B*). The collision artificially prolonged the swing phase, producing the relationship seen. If we discount the results from the trailing leg because of the mechanical artifact, the remaining relationships (Fig. 2.4A-C) are remarkably similar.

2.4.3 Muscle Activation Patterns in Different Directions of Stepping

The similarity in EMG patterns between different directions of stepping was not predicted by early hypotheses on how a locomotor CPG could mediate different forms of stepping. Grillner (1981) originally theorized that the locomotor CPG was organized such that the switch from forward to backward walking would be achieved by a switch in coupling between the hip and knee joint muscles. However, subsequent findings in intact cats and adult humans have not been consistent with this theory (Thorstensson 1986; Winter et al. 1989; Buford and Smith 1990; Grasso et al. 1998). In intact cats, basic muscle synergies are similar for forward and backward walking (Buford and Smith 1990). Generally, single-joint flexors were active during swing and single-joint extensors were active during stance. While the motor patterns of single-joint muscles were well conserved, the changes in the pattern of bifunctional muscles with different forms of cat locomotion are more complex. Similarly, in infants, we found that the flexor muscles are generally active during swing and the extensor muscles are generally active during stance for all directions of stepping along a 180° path. The exception was the switch in the activity pattern of the hamstrings muscles in backward stepping compared to the other directions of stepping. This type of switch has been reported in detail in many other bifunctional muscles in the cat (Pratt et al. 1996). Pratt et al. (1996) suggested that the differences seen between forward and backward walking in bifunctional muscle patterns are due to the greater complexity of their function and presumably the greater complexity in their inputs from central and peripheral sources. They propose that the greater number of output options available to multi-joint muscles allow for a better ability to meet the mechanical demands of the task. Unfortunately, we cannot differentiate the specific functions of bifunctional muscles using surface EMG recordings from human infants because of the small dimensions of the infants' legs.

The EMG patterns were statistically different for a small number of comparisons. Many trends were noted, however, which could be physiologically important. For example, the extensors from the trailing leg were consistently lower than forward stepping, while the flexors from the leading leg were consistently higher. This suggests that the role played by the leading and trailing legs were asymmetric compared to forward stepping. In forward and backward stepping, the hamstring muscle clearly plays a different role (as discussed above), but the ankle plantarflexors and knee extensors might also have slightly different roles to play. For example, the push-off burst in the plantarflexors is absent, and the quadriceps activity is more prolonged in the stance phase during backward stepping.

Whatever the differences in the EMG patterns, they do not affect our main conclusion, that the different directions of infant stepping are likely produced by similar circuitry. There is ample evidence that the same circuitry can produce radically different movement patterns in other animals (e.g. Marder and Calabrese 1996; Stein et al. 1998). It is curious that the EMG patterns from infants stepping in different directions are so similar. This is in contrast to some of the results from adults and from other animals (e.g. Thorstensson 1986; Buford and Smith 1990; Trank et al. 1996; Grasso et al. 1998). It is possible that many of the differences seen in other animals and adult humans are related to the change in the role of the muscles to produce propulsion and postural adjustments for the different directions of walking. These infants are held over a treadmill, so that the need for propulsion and postural control are much reduced. These mechanical factors could account in part for the differences observed between infants compared to adult humans and cats.

2.4.4 Backward and Forward Walking are Different between Infants and Adults

The existing literature on forward and backward walking in higher vertebrates has been focused on intact preparations (i.e. adult humans and cats) (Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). The changes in EMG pattern that occur with change in direction in adult human walking are quite irregular (Grasso et al. 1998). Indeed, findings are also variable between the laboratories which have examined motor patterns in adult forward and backward walking (cf. Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). However, there are other factors likely influencing locomotor output that need to be taken into account when considering backward and forward walking in adult humans and intact cats. Buford et al. (1990) and Buford and Smith (1990) emphasize the postural adaptations that are required for backward walking in cats. The key role of posture in regulating motor patterns during cat locomotion is also highlighted in studies of crouched walking and slope walking (Trank et al. 1996; Carlson-Kuhta 1998; Smith et al. 1998a). In adult humans, Grasso et al. (1998) argue that rather than having a strict regulation of EMG patterns, locomotion is more highly controlled via limb segment motion. If the movement trajectory of backward walking is reversed in time, it is very similar to that of forward walking (Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). In their scheme, Grasso et al. (1998) propose that the control of muscle activity is secondary to the attainment of the behavioural goals of the nervous system. Thus, in intact cats and adult humans, it appears that the regulation of backward walking is governed by other factors such as postural control or limb joint motion while the regulation of muscle activity patterns occurs secondarily to the execution of these functions.

The infants we studied, all under 12 months of age, likely have minimal cerebral influence directing their motor output (Koh and Eyre 1988; Müller et al. 1991). In addition, the infants were supported while stepping on the treadmill, and presumably factors such as equilibrium did not influence their stepping. Compared to adults, the EMG in infant stepping is less variable between subjects and between different directions (Fig. 2.7). This is quite different from the inter-subject (Grasso et al. 1998) and inter-laboratory variability in EMG patterns between backward and forward walking in adults (cf. Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). On the other hand, limb joint motion in adult humans is very similar between backward and forward walking while it is quite different in infants. Why were the kinematics different (between forward and backward stepping) while the EMGs similar? The kinematic differences were seen mostly at the hip and knee. First, there are some apparent differences in the EMGs of the GS and QUAD, even though statistically, they were not different. Second, we were recording the gross activity of 4 large muscle groups only. The differences seen in the hamstrings likely produced some of the large differences seen at the knee. We have not recorded from any of the single joint hip muscles (because of technical difficulties), which are likely to have a very important role in the limb movement particularly during swing phase. Together, we feel these factors could account for the kinematic differences seen. Since motor cortical function is immature in infants, the precise regulation of limb joint motion in adults in contrast to that in infant stepping suggests that the control of kinematic variables seen in adults originate from higher brain centres.

2.4.5 Conclusions

We feel that the present data is consistent with the idea that a common locomotor CPG controls stepping in all different directions in infants. We cannot exclude the possibility that a separate CPG exists for each direction of stepping. While a separate CPG may exist for forward and backward walking and conceivably even a third CPG for sideways walking, it seems quite unlikely that separate locomotor CPGs exist for all possible directions of walking (theoretically an infinite number of directions). There was little that made one direction of stepping stand out from the others. There was a similarity in the response to changes in treadmill speed, regardless of the direction of stepping. Furthermore, there were no discrete changes in either EMG phasing patterns or the temporal parameters of stepping as the direction of stepping was gradually changed. While the data presented here cannot directly reveal the nature of the neural circuits involved, they are compatible with the idea that a common central pattern generator could govern locomotion in different directions.

2.5 References

Buford JA, Smith JL. Adaptive control for backward quadrupedal walking. II. Hindlimb muscle synergies. *Journal of Neurophysiology* 64: 756-766, 1990.

Buford JA, Zernicke RF, Smith JL. Adaptive control for backward quadrupedal walking. I. Posture and hindlimb kinematics. *Journal of Neurophysiology* 64: 745-755, 1990.

Carlson-Kuhta P, Trank TV, Smith JL. Forms of forward quadrupedal locomotion. II. A comparison of posture, hindlimb kinematics, and motor patterns for upslope and level walking. *Journal of Neurophysiology* 79: 1687-1701, 1998.

Eyre JA, Miller S, Ramesh V. Constancy of central conduction delays during development in man: investigation of motor and somatosensory pathways. *Journal of Physiology* 434: 441-452, 1991.

Flament D, Goldsmith P, Lemon RN. The development of corticospinal projections to tail and hindlimb motoneurons studied in infant macaques using magnetic brain stimulation. *Experimental Brain Research* 90:225-228, 1992a

Flament D, Hall EJ, Lemon RN. The development of cortico-motoneuronal projections investigated using magnetic brain stimulation in the infant macaque. *Journal of Physiology* 447: 755-768, 1992b.

Forssberg H. Ontogeny of human locomotor control. I. Infant stepping, supported locomotion and transition to independent locomotion. *Experimental Brain Research* 57: 480-493, 1985.

Getting PA. Emerging principles governing the operation of neural networks. *Annual Reviews in Neuroscience* 12: 185-204, 1989.

Glass GV, Hopkins KD. *Statistical Methods in Education and Psychology*, 3rd ed. Needham Heights, MA: Allyn and Bacon, 1996.

Grasso R, Bianchi L, Lacquaniti F. Motor patterns for human gait: backward versus forward locomotion. *Journal of Neurophysiology* 80: 1868-1885, 1998.

Grillner S. Control of locomotion in bipeds, tetrapods, and fish. In: *Handbook of Physiology. Section 1: The Nervous System, Volume II. Motor Control, Part 2,* edited by JM Brookhart and VB Mountcastle. Bethesda, MD: American Physiological Society, 1981, pp. 1179-1236.

Grillner S. Neurobiological bases of rhythmic motor acts in vertebrates. *Science* 228: 143-149, 1985.

Hall E, Flament D, Bennett K, Lemon RN. Anatomical and behavioral parallels in the development of the corticospinal tract. In: *Tutorials in Motor Behavior II,* edited by GE Stelmach and J Requin. Amsterdam: Elsevier Science Publishers, 1992, pp. 861-875.

Halverson HM. The development of prehension in infants. In: *Child Behavior and Development.* New York, NY: McGraw-Hill, 1943, pp. 49-65.

Koh THHG, Eyre JA. Maturation of corticospinal tracts assessed by electromagnetic stimulation of the motor cortex. *Archives of Disease in Childhood* 63: 1347-1352, 1988.

Marder E, Calabrese RL. Principles of rhythmic motor pattern generation. *Physiological Reviews* 76: 687-717, 1996.

Matsushima T, Grillner S. Neural mechanisms of intersegmental coordination in lamprey: local excitability changes modify the phase coupling along the spinal cord. *Journal of Neurophysiology* 67: 373-388, 1992a.

Matsushima T, Grillner S. Local serotonergic modulation of calcium-dependent potassium channels controls intersegmental coordination in the lamprey spinal cord. *Journal of Neurophysiology* 67: 1683-1690, 1992b.

Mortin LI, Keifer J, Stein PSG. Three forms of the scratch reflex in the spinal turtle: movement analyses. *Journal of Neurophysiology* 53: 1501-1516, 1985.

Mortin LI, Stein PSG. Spinal cord segments containing key elements of the central pattern generators for three forms of scratch reflex in the turtle. *Journal of Neuroscience* 9: 2285-2296, 1989.

Müller K, Hömberg V, Lenard HG. Magnetic stimulation of motor cortex and nerve roots in children. Maturation of cortico-motoneuronal projections. *Electroencephalography Clinical Neurophysiology* 81: 63-70, 1991.

Pedhazur EJ. *Multiple Regression in Behavioral Research*, 2nd ed. New York: CBS College Publishing, 1982.

Peiper A. *Cerebral Function in Infancy and Childhood*. New York, NY: Consultants Bureau, 1963.

Pratt CA, Buford JA, Smith JL. Adaptive control for backward quadrupedal walking. V. Mutable activation of bifunctional thigh muscles. *Journal of Neurophysiology* 75: 832-842, 1996.

Robertson GA, Mortin LI, Keifer J, Stein PSG. Three forms of the scratch reflex in the spinal turtle: central generation of motor patterns. *Journal of Neurophysiology* 53: 1517-1534, 1985.

Smith JL, Chung SH, Zernicke RF. Gait-related motor patterns and hindlimb kinetics for the cat trot and gallop. *Experimental Brain Research* 94: 308-322, 1993.

Smith JL, Carlson-Kuhta P. Unexpected motor patterns for hindlimb muscles during slope walking in the cat. *Journal of Neurophysiology* 74: 2211-2215, 1995.

Smith JL, Carlson-Kuhta P, Trank TV. Forms of forward quadrupedal locomotion. III. A comparison of posture, hindlimb kinematics, and motor patterns for downslope and level walking. *Journal of Neurophysiology* 79: 1702-1716, 1998a.

Smith JL, Carlson-Kuhta P, Trank TV. Motor patterns for different forms of walking: cues for the locomotor central pattern generator. *Annals of the New York Academy of Sciences* 860 : 452-455, 1998b.

Stein PSG, Smith JL. Neural and biomechanical control strategies for different forms of vertebrate hindlimb motor tasks. In: *Neurons Networks and Motor Behavior*, edited by PSG Stein, S Grillner, AI Selverston, and DG Stuart. Cambridge, MA: MIT Press, 1997, pp. 61-73.

Stein PSG, Mortin LI, Robertson GA. The forms of a task and their blends. In: *Neurobiology of Vertebrate Locomotion*, edited by S Grillner. London, UK: Macmillan, 1986, pp. 201-216.

Stein PSG, McCullough ML, Currie SN. Reconstruction of flexor/extensor alternation during fictive rostral scratching by two-site stimulation in the spinal turtle with a transverse spinal hemisection. *Journal of Neuroscience* 18: 467-479, 1998.

Tegnér J, Matsushima T, El Manira A, Grillner S. The spinal GABA system modulates burst frequency and intersegmental coordination in the lamprey: differential effects of $GABA_A$ and $GABA_B$ receptors. *Journal of Neurophysiology* 69: 647-657, 1993.

Thorstensson A. How is the normal locomotor pattern modified to produce backward walking? *Experimental Brain Research* 61: 664-668, 1986.

Trank TV, Chen C, Smith JL. Forms of forward quadrupedal locomotion. I. A comparison of posture, hindlimb kinematics, and motor patterns for normal and crouched walking. *Journal of Neurophysiology* 76: 2316-2326, 1996.

Vilensky JA, Gankiewicz E, Gehlsen G. A kinematic comparison of backward and forward walking in humans. *Journal of Human Movement Studies* 13: 29-50, 1987.

Winter DA, Pluck N, Yang JF. Backward walking: a simple reversal of forward walking? *Journal of Motor Behavior* 21: 291-305, 1989.

Yakovlev PI, Lecours A-R. The myelogenetic cycles of regional maturation of the brain. In: *Regional Development of the Brain in Early Life*, edited by A Minkowski. Oxford, UK: Blackwell, 1967, pp. 3-70.

Yang JF, Stephens MJ, Vishram R. Infant stepping: a method to study the sensory control of human walking. *Journal of Physiology* 507: 927-937, 1998a.

Yang JF, Lamb T, Vishram R. Human infants walk backwards and sideways with support, and adjust to different walking speeds. *Society for Neuroscience Abstracts* 24: 2107, 1998b.

CHAPTER 3

PROPRIOCEPTIVE MODULATION OF HIP FLEXOR ACTIVITY DURING THE SWING PHASE OF LOCOMOTION IN DECEREBRATE CATS

Adapted from an original publication:
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3.1 Introduction

The importance of proprioceptive afferent feedback during locomotion is well established (reviewed in Rossignol 1996; Duysens et al. 2000). This has been demonstrated most clearly for the extensor system in a variety of preparations where length- and load-sensitive afferent signals from the legs have been found to be key for the control of extensor activity and the transition to the swing phase (reviewed in Orlovsky et al. 1999). In decerebrate walking cats, it has been found that extensor burst duration is regulated by load-sensitive afferents from extensor muscles (Duysens and Pearson 1980; Whelan et al. 1995) and by stretch-sensitive afferents from flexor muscles (Hiebert et al. 1996). Extensor burst amplitude is controlled largely by feedback from length- and force-sensitive afferents in the extensor muscles (see Pearson 1995 for review).

Investigations on the modulation of the swing phase by muscle afferents have so far been limited. Much of the literature regarding peripheral afferent modulation of the swing phase has focused on the role of cutaneous afferents (reviewed in Rossignol 1996). Few reports have presented evidence that proprioceptive inputs from non-cutaneous sources influence the swing phase. Orlovskii and Shik (1965) put forth this concept in their study of the response to elbow braking during treadmill locomotion in dogs. Despite an applied braking force during swing, the forelimb was able to rapidly compensate and resume forward advancement with the speed and inter-joint coordination as during undisturbed stepping. There was a 30 ms delay from the time of braking to the time that a correction was observed. This short delay suggested that the mechanism used to stabilize limb trajectory during swing is realized at relatively low levels of the nervous system (Orlovskii and Shik

1965). Thus, they contended that segmental mechanisms exist which serve to ensure a relatively standard swing phase in order for safe paw placement and support to occur.

Involvement of flexor muscle afferents during the swing phase is also indicated from results of experiments using decerebrate cat treadmill locomotion and fictive locomotion (Perreault et al. 1995; Hiebert et al. 1996; McCrea et al. 2000; Quevedo et al. 2000). Perreault et al. (1995) have reported that stimulation of afferents from sartorius, tibialis anterior (TA), and semitendinosus muscles at group I strength during flexion can prolong the flexor phase during fictive locomotion while stimulation at group II strength during flexion consistently terminated flexion and reset the rhythm to extension. Recently, however, McCrea et al. (2000) reported that afferents from iliopsoas and sartorius muscles stimulated at both group I and II strengths can prolong and enhance ongoing flexion. Existence of a group I disynaptic excitatory pathway to flexor motoneurons has also recently been demonstrated during fictive locomotion (Degtyarenko et al. 1998; Quevedo et al. 2000). During decerebrate treadmill stepping, stimulation of the nerve to the extensor digitorum longus (EDL) muscle at both group I and II strengths can increase the duration of flexion (Hiebert et al. 1996). TA stimulation at group II strength can also prolong flexor activity (Hiebert et al. 1996). Thus, previous results from fictive and decerebrate cat locomotion have demonstrated an influence from flexor muscle afferents onto the locomotor central pattern generator (CPG) and thus indicate a role for these afferents in modulating the swing phase.

The purpose of this study was to determine whether afferent feedback from hip flexor muscles is involved in the modulation of flexor activity in walking decerebrate cats. Using natural stimuli to perturb flexor muscle contractions, we show that modifying the feedback from hip flexor muscles, particularly the sartorius muscles, can have a powerful influence on the amplitude and duration of flexor burst activity. Preliminary results from this study have been published in abstract form (Lamb and Pearson 2000).

3.2 Methods

The data presented in this paper were obtained from experiments on 16 adult cats of both sexes. All procedures were approved by the University of Alberta Health Sciences Animal Welfare Committee.

3.2.1 Preparation

Animals were initially anesthetized with halothane. The trachea was then cannulated for the continuous administration of the anesthetic. One carotid artery was ligated and the other cannulated for monitoring the blood pressure. One jugular vein was cannulated for the administration of drugs. Intramuscular fine-wire recording electrodes (Cooner Wire AS632, Cooner Wire Company, Chatsworth, CA) were sewn into the following muscles of the left hindlimb: iliopsoas (IP), anterior head of sartorius (SartA), medial head of sartorius (SartM), and medial gastrocnemius (MG). Electrodes were also sewn into the IP and MG muscles on the right side. Electrode leads were threaded under the skin to a connector located externally on the animal's back. To eliminate cutaneous input and afferent input from other muscles, the following nerves were cut: the two branches of the sural, saphenous, distal tibial, femoral (distal to the sartorius nerve) and either the deep and superficial peroneal (distal to its branch to the tibialis anterior muscle) or the common peroneal nerve. In 1 animal, the cranial and caudal gluteal nerves were also cut. The hamstrings nerve was cut in 5 animals and the obturator nerve was cut in 4 animals.

The nerves to the SartA and SartM muscles were identified and looped off with a thread (n = 8 animals). This enabled us to examine the specific role of the sartorius muscles during swing by blocking conduction in their nerves when the looped thread was tied off and pulled. Interruption of the nerve supply to the sartorius muscles was confirmed by the elimination of sartorius electromyographic (EMG) signals. In a number of animals (n = 15), a hole was drilled into the tibia about 6 cm above the ankle joint and a screw inserted. The screw served as the distal anchor for the blocking device (described below).

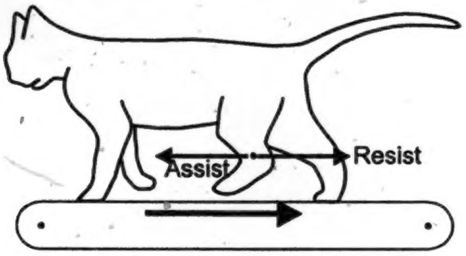
After these procedures, the animal was placed over a motorized treadmill and fixed in a stereotaxic frame. The animal was then decerebrated by transecting the brainstem at a 50° angle from the anterior edge of the superior colliculus. The anesthesia was discontinued at this time. Within an hour, spontaneous stepping usually occurred in response to the moving treadmill belt. The speed of the treadmill was set between 0.3 and 0.4 m/s. Manual stimulation to the perineum was sometimes used to evoke stepping. When spontaneous treadmill locomotion could not be consistently evoked, electrical stimulation of the mesencephalic locomotor region (MLR) was used (n = 8 animals). Typical stimulus parameters were 15 Hz, 0.5 ms pulses, 100–200 μA. Generally, locomotion generated by MLR stimulation shares many characteristics of locomotion in intact animals (Shik et al. 1966). We did not observe any overall qualitative differences between the locomotor pattern of spontaneously and MLR-evoked walking animals. Thus, the data were combined and presented as a group.

Perturbations to swing of the left leg were applied in one of two ways: manual resistance or assistance (Fig. 3.1A) or blocking hip flexion (Fig. 3.1*B*). Resistance was applied manually by the experimenter holding the ankle during the swing phase and applying a force opposing the swinging limb. Assistance was applied in the same way except the limb was pushed forward during swing. During the manual perturbation trials, the experimenter maintained light hold of the ankle to avoid interfering with normal stepping sequences but at the same time prepared to administer a perturbation. Manual perturbations during swing were applied rhythmically and synchronized with the naturally occurring flexor burst activity. The manual perturbations lasted for less than or more than the normal swing duration during assistance and resistance, respectively, as estimated by the experimenter holding the limb. In order to ensure that excessive force was not used to manually perturb the limb, we videotaped an experimental session in one animal with markers on the trunk, hip, and knee joints. Joint angles were measured using these markers and we found that the excursion of the hip joint did not differ greatly between the different conditions, based on data from 20 randomly chosen steps in each condition. During undisturbed stepping, the movement of the hip joint ranged from an extended position of -7.3 ± 3.4°(mean ± SD) to a flexed position of 30.0 ± 1.9°. During manual assistance, the range was from -4.2 ± 3.3° to 35.5 ± 2.5°. During manual resistance, the position of the hip tended toward extension, from -15.2 ± 2.0° to 14.2 ± 5.7°. In this animal, the manual assistance perturbations that were applied were approximately from 50 to 150 ms less than the normal swing duration. The manual resistance perturbations were approximately 100 to 150 ms more than the normal swing duration.

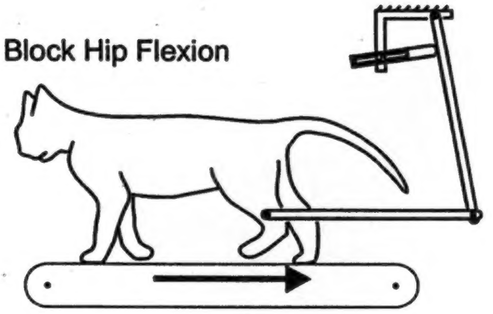
Figure 3.1. Illustrations of the Experimental Preparation used to Apply Perturbations during the Swing Phase.

A. Manual resistance or assistance to swing. *B*. Blocking device used to apply resistance to the swinging limb. C. Schematic diagram of the hip flexor muscles examined in this study.

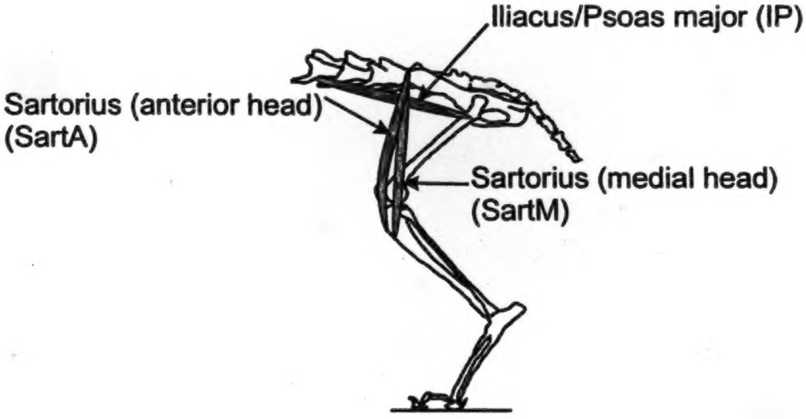
A. Manual Perturbation to Swing


Assist
Resist

B. Block Hip Flexion



C.


Iliacus/Psoas major (IP)
Sartorius (anterior head) (SartA)
Sartorius (medial head) (SartM)

The use of the blocking device (Fig. 3.1*B*) allowed better timing of the resistance to swing. This device allowed leg extension but firmly prevented full flexion at the hip. The device's position could be adjusted such that hip flexion could be blocked at various times during the swing phase. A force transducer coupled with the device allowed measurement of the time of the onset of the block.

3.2.2 Data Analysis

The analog data (raw EMG signals and force transducer signal) were recorded on tape using a Vetter 4000A PCM machine. A hard copy of the data was printed out using a Gould TA11 chart recorder from which sequences of regular consistent stepping were identified (usually 10 to 20 steps). The EMG analog data were filtered with a band-pass filter (high pass 10 Hz, low pass 30 Hz) and full-wave rectified. The force signal was filtered at a low-pass frequency of 30 Hz. Each EMG channel and the force signal were then digitized at a sampling rate of 500 Hz and stored on computer using a data acquisition system (Axotape 2.0.2, Axon Instruments). Custom written computer software programs were used to average and plot the digitized EMG traces, measure burst amplitude, and measure burst duration and cycle period. The amplitude of the EMG signal was calculated as the average amplitude over the whole duration of each burst for each muscle. Cycle duration was defined as the time from the onset of an IP burst to the next IP burst. Average burst durations and flexor burst amplitudes were calculated for undisturbed and perturbed trials from stepping sequences from each animal. Any response in the EMG burst duration or amplitude to the perturbations was expressed as a percentage of the average duration or amplitude of a previous sequence of undisturbed stepping. Descriptions in the text of "burst activity" refer to both amplitude and duration. The onset of blocking hip flexion was measured as the interval between the onset of the IP burst and the onset of force indicated by the force transducer signal. Student's *t*-tests were used to determine significant differences and the level of significance was set at 0.05.

3.3 Results

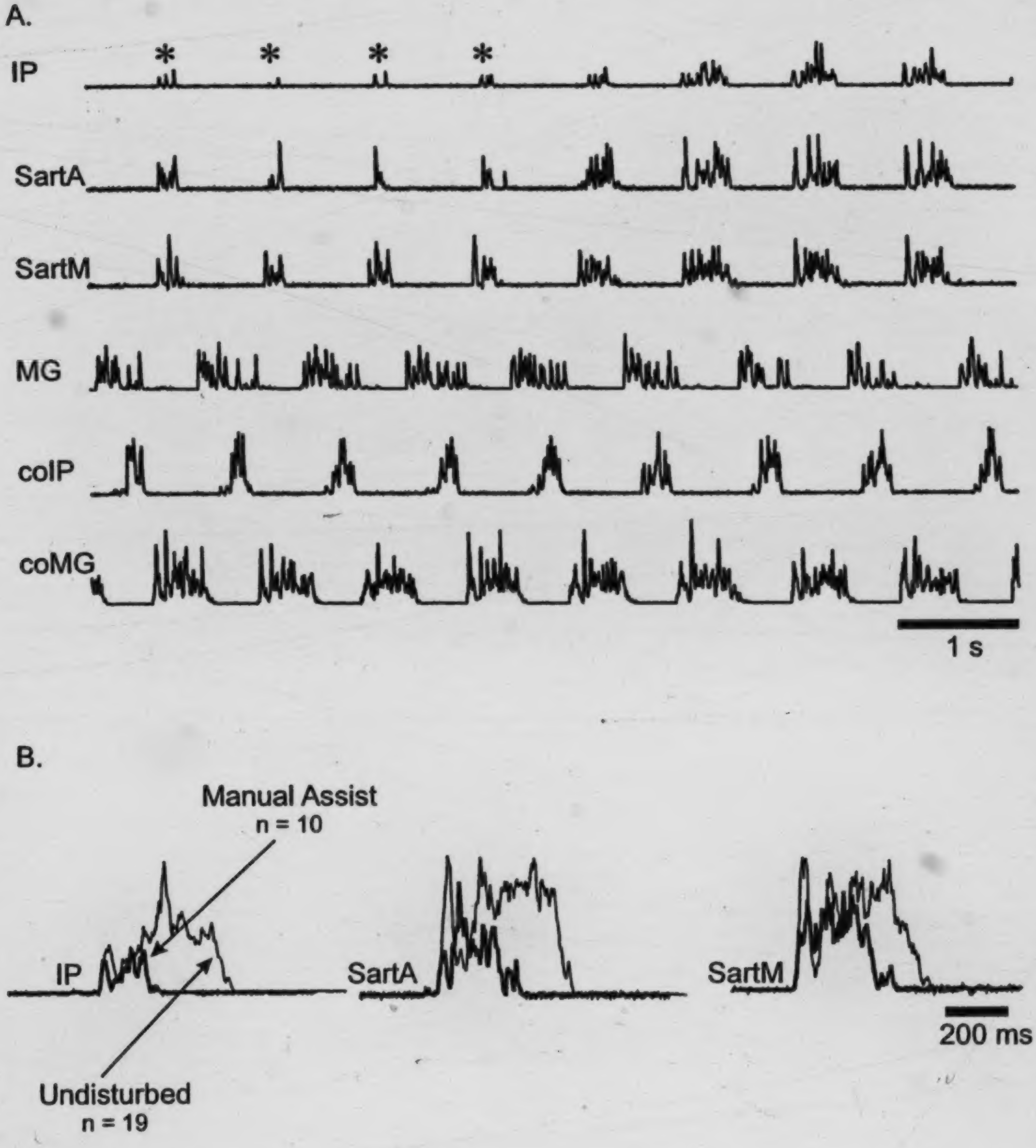
3.3.1 Sensory Input from Hip Flexor Muscles Influences Flexor Burst Activity

In this study, we present data demonstrating that sensory input from hip flexor muscles during the swing phase can modify the amplitude and duration of burst activity in flexor muscles. The flexor muscles we focused on were the iliopsoas and the two heads of sartorius (Fig. 3.1C). All effects were obtained from the partially denervated hindlimbs of decerebrate cats during treadmill locomotion. The denervation eliminated cutaneous input as well as afferent input from most other muscles in the hindlimb.

Manual assistance to hip flexion was applied to advance hip flexion during decerebrate walking (n = 7). Data from a representative animal is shown in figure 3.2. Figure 3.2A shows a sequence of continuous stepping during which manual assistance was applied (denoted by asterisks) followed by undisturbed, control stepping. Once manual assistance was discontinued, flexor burst activity returned to control. In addition, contralateral stepping remained consistent throughout the disturbances and afterwards. Averaged flexor bursts are shown in figure 3.2*B* (averages were taken from the same sequence of steps that is partially shown in the example in fig. 3.2A). The major effect was the decrease in flexor burst duration when manual assistance to hip flexion was applied.

Figure 3.2. Effect of Manual Assistance during Swing.

A. Rectified and filtered EMG records illustrate the reduction in ipsilateral hip flexor activity due to manual assistance (indicated by *). *B.* Averaged EMG records for the hip flexor muscles from the same stepping sequence which is partially shown in A. Thick trace, manually assisted steps. Thin trace, undisturbed stepping. Abbreviations: IP, iliopsoas; SartA, sartorius (anterior head); SartM, sartorius (medial head); MG, medial gastrocnemius; coIP, contralateral iliopsoas; coMG, contralateral medial gastrocnemius.


A.
* * * *
IP
SartA
SartM
MG
coIP
coMG
1 s
B.
Manual Assist
n = 10
IP
SartA
SartM
Undisturbed
n = 19
200 ms

When manual resistance was applied to prevent hip flexion during decerebrate walking (n = 7), a significant increase in flexor burst activity was observed. A representative example of the response to manual resistance to hip flexion from a single cat is illustrated in figure 3.3 (same animal as in Fig. 3.2). The response to manual resistance was opposite of that observed during manual assistance. Figure 3.3A shows a sequence of undisturbed stepping followed by a bout of stepping during which manual resistance was applied. The increase in activity in the flexor bursts was apparent as soon as the manual resistance was applied (denoted by asterisks). In figure 3.3B, averaged flexor bursts are illustrated (averages were taken from the same sequence of steps that is partially shown in the example in fig. 3.3A). In this example, there was an increase in duration in all muscles and an increase in IP burst amplitude during manual resistance.

In figure 3.4A, the average decrease in the duration of the flexor bursts in response to manual assistance for each of the 7 animals is illustrated. To eliminate the possibility that reciprocal inhibition from the hip extensor muscles could account for the effects seen during manual assistance, the hamstrings muscles were denervated in 2 cats (JE and M6, indicated by asterisk). In 1 cat (MI, indicated by double asterisks), both the hamstrings and the gluteal nerves were cut. No difference in the response to manual assistance to hip flexion was seen between the animals with the hip extensors denervated and those with them intact ($p > 0.10$). Figure 3.4B illustrates the average increase in the duration of the flexor bursts in response to manual resistance.

An obvious limitation to the manual perturbations is the inability to precisely regulate the timing and amplitude of the resisting or assisting movement. To address this issue, we devised a mechanical blocking device (illustrated in Fig. 3.1B). This allowed us to

Figure 3.3. Effect of Manual Resistance during Swing.

A. Rectified and filtered EMG records illustrate the increase in ipsilateral hip flexor activity due to manual resistance (indicated by *). *B.* Averaged EMG record for hip flexor muscles from the same stepping sequence which is partially shown in A. Thick trace, manually resisted steps. Thin trace, undisturbed stepping. Abbreviations are the same as in previous figures.

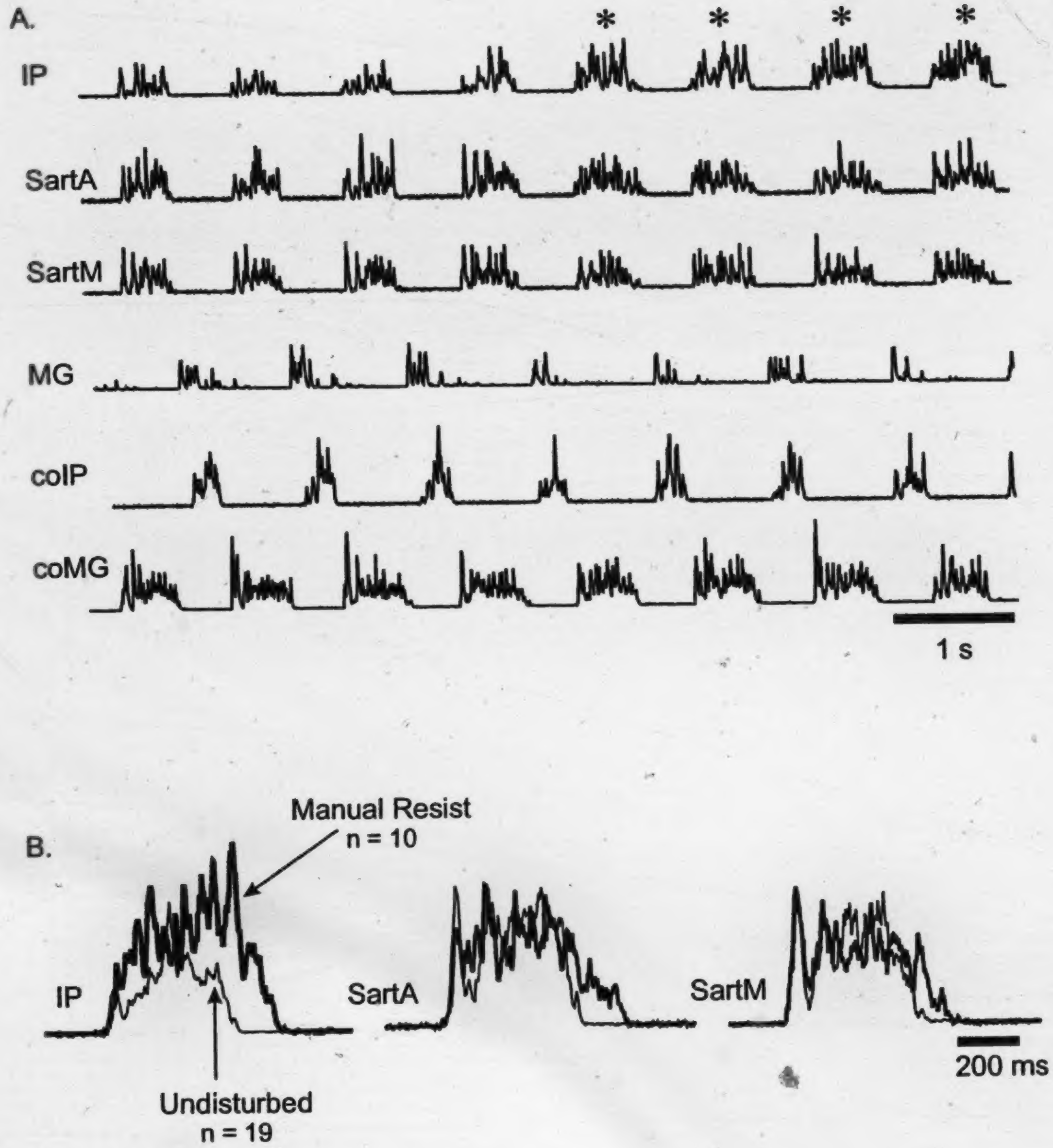
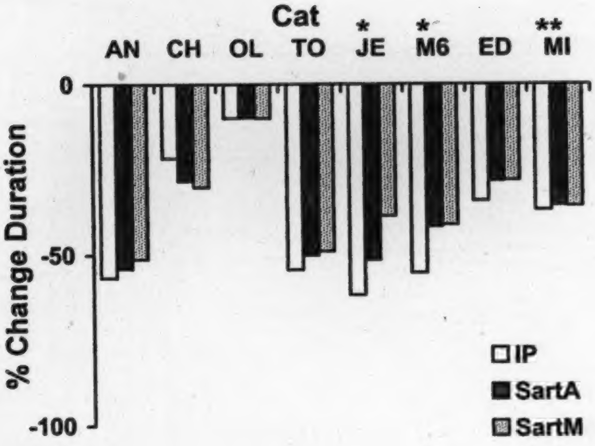

A.
*
*
*
*
IP
SartA
SartM
MG
coIP
coMG
1 s
B.
Manual Resist
n = 10
IP
SartA
SartM
Undisturbed
n = 19
200 ms

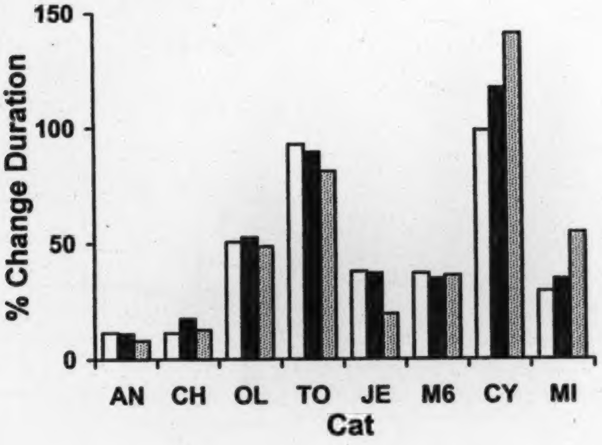
Figure 3.4. Group Data for the Response to Manual Perturbations.

A. Percent reduction in flexor burst duration for each cat in response to manual assistance. The hamstrings nerve was cut in "JE" and "M6" (denoted by *) and the gluteal nerves were cut in "MI" (denoted by **). Their response to manual assistance was similar to that observed in other cats. Thus, reciprocal inhibition due to rapid stretch of the hip extensors likely does not have a major role in this response. *B*. Percent increases in flexor burst duration for each cat due to manual resistance.

A. Manual Assistance



B. Manual Resistance

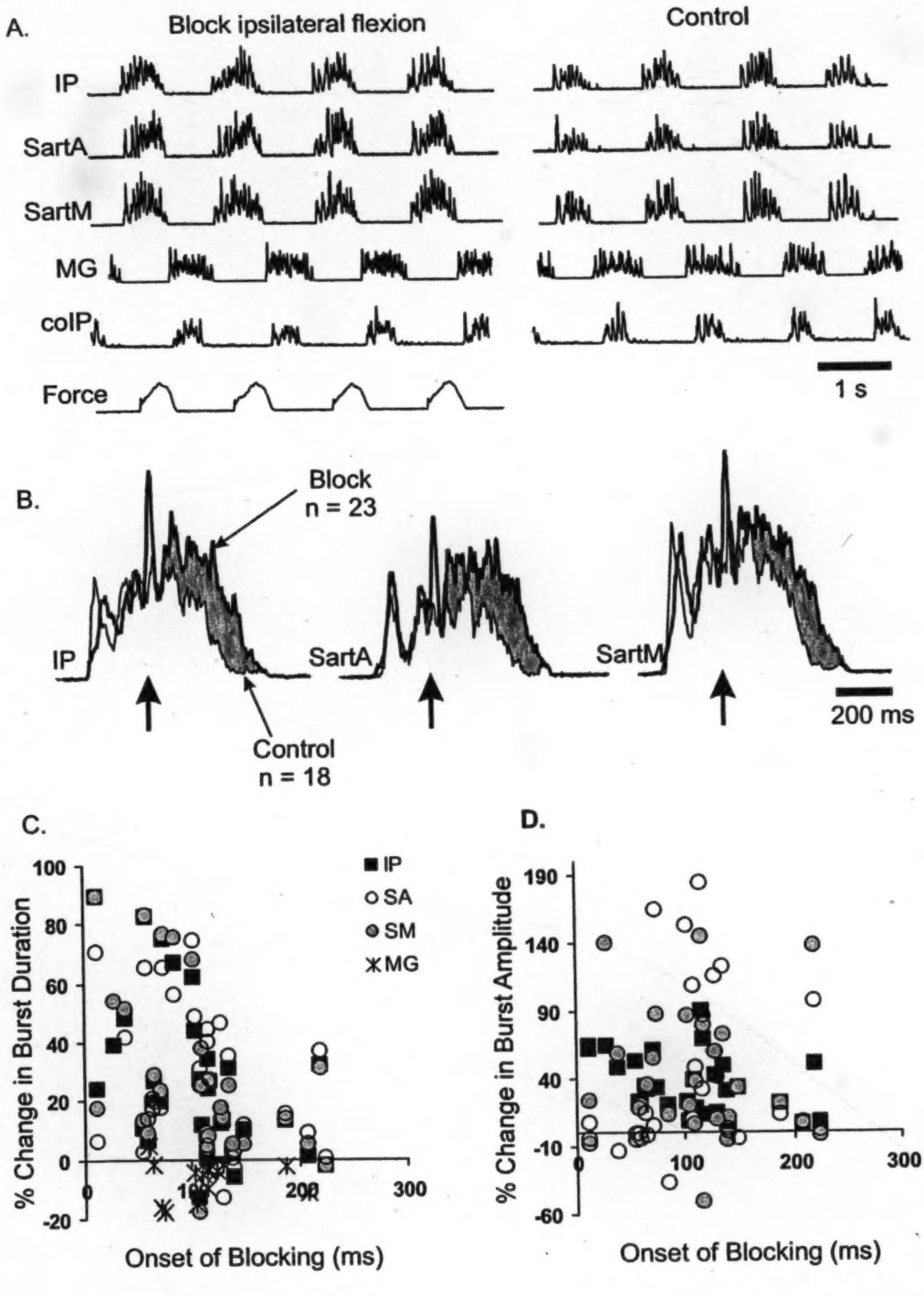


block hip flexion at different times during the swing phase. Data from 13 animals were collected while blocking hip flexion in this way.

Similar to the effects of manual resistance, blocking hip flexion resulted in an increase in duration and amplitude of the flexor bursts. An example of the response to the mechanical blocking device is shown in figure 3.5. In figure 3.5A, the response to blocking hip flexion is illustrated in rectified and filtered EMG records of adjacent stepping sequences, during which flexion was blocked in the first sequence, followed by a sequence of undisturbed stepping. The increase in the duration of the flexor bursts as well as an accompanying decrease in MG burst duration is apparent. Figure 3.5*B* illustrates averaged flexor bursts from the same stepping sequence shown in figure 3.5A. During this sequence, the onset of the force occurred 190 ms after the onset of the IP burst (denoted by black arrows). There was a short burst of activity, presumably a short-latency reflex response, occurring after the onset of the block. Following this, there was a general increase in both flexor burst duration and amplitude (shaded area). There was also a general trend for a relationship between the onset time of blocking flexion and the degree of increase in flexor burst duration (Fig. 3.5C). In other words, the largest increase in flexor burst duration tended to occur when blocking of the limb occurred earlier in the flexor phase of locomotion. The duration of the MG bursts also tended to be lower when hip-flexion was blocked compared to undisturbed stepping. The increase in flexor burst amplitude was not related to the time of onset of the block (Fig. 3.5*D*). Each point in the scatterplots in figures 5C and D represent the mean change in flexor burst duration or amplitude (compared to control) of a sequence of stepping during which hip flexion was blocked at a given time.

Figure 3.5. Effect of Blocking Hip Flexion during Swing.

A. Rectified and filtered EMG records and force trace indicating the onset of force perturbation during each step cycle. B. Averaged EMG records from hip flexor muscles from the same cat shown in A. Thick trace, blocked steps. Thin trace, undisturbed stepping. Abbreviations are the same as in previous figures. Arrow indicates the onset of blocking hip flexion. Blocking hip flexion causes an increase in both amplitude and duration of flexor bursts (shaded area). C. Percent change in burst duration and amplitude plotted as a function of the onset of blocking hip flexion. The percent increase in hip flexor burst duration had a trend of decreasing as the onset of blocking hip flexion occurred later in the swing phase. MG burst duration also tended to be lower when hip flexion was blocked. There was no trend observed in the change in flexor burst amplitude with the timing of blocking hip flexion.


A.
Block ipsilateral flexion
Control
IP
SartA
SartM
MG
coIP
Force
1 s
B.
Block
n = 23
IP
SartA
SartM
Control
n = 18
200 ms
C.
% Change in Burst Duration
100
80
60
40
20
0
-20
0
100
200
300
IP
SA
SM
MG
Onset of Blocking (ms)
D.
% Change in Burst Amplitude
190
140
90
40
-10
-60
0
100
200
300
Onset of Blocking (ms)

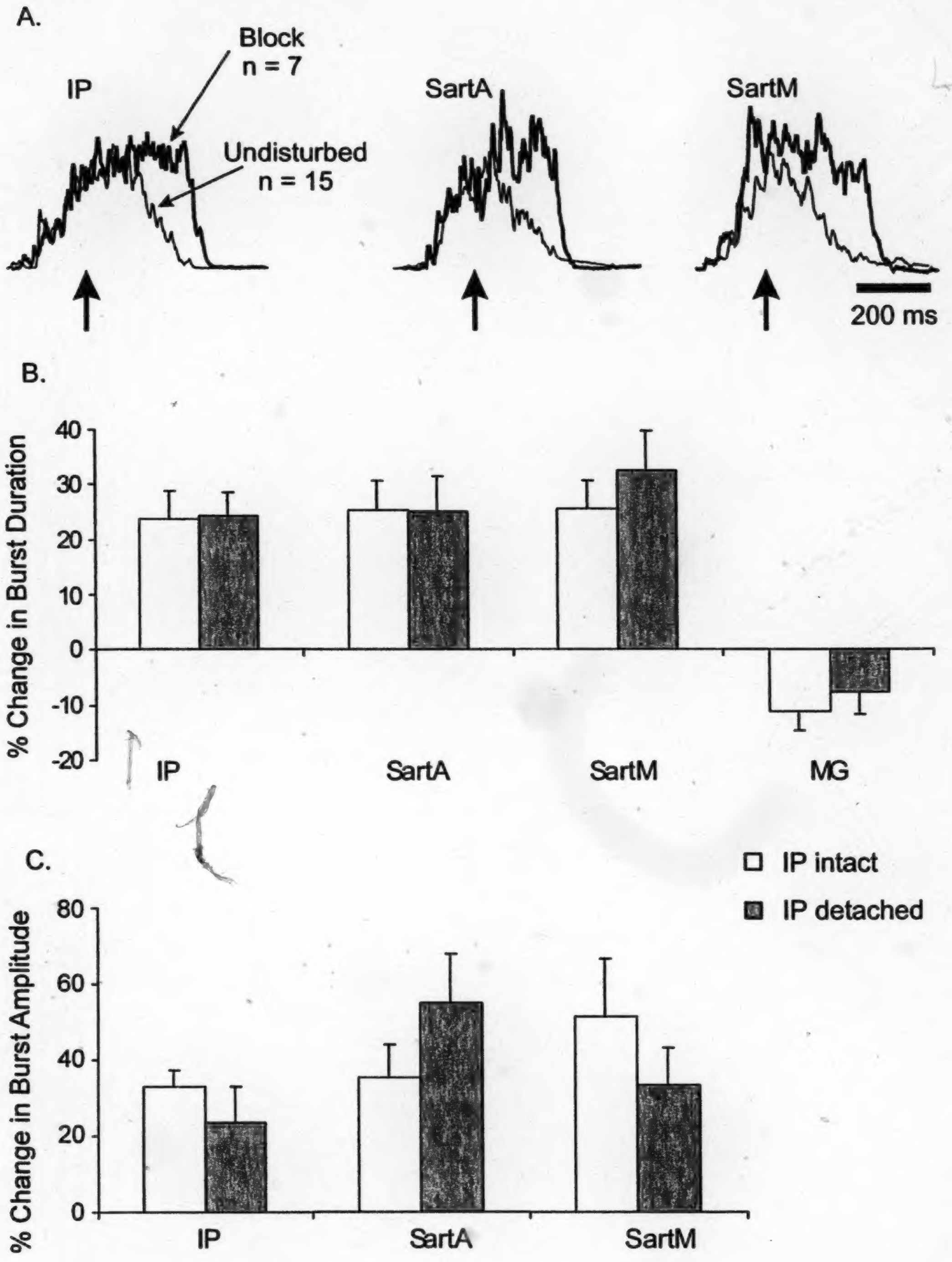
3.3.2 Afferents from the Sartorius Muscles are Particularly Important for Flexor Burst Modulation

In order to differentiate the roles of the hip flexor muscles, we performed a series of experiments where either the IP muscle was detached from its insertion or conduction was blocked in the nerves to the SartA and SartM muscles. Unfortunately, due to technical constraints, the IP muscle had to be detached from its insertion before treadmill locomotion could be elicited. Thus, in these experiments, the animal could not serve as its own control for examining the effect of IP tenotomy.

In 5 experiments, we detached the IP tendon from its distal attachment, effectively leaving the SartA and SartM muscles as the major hip flexor muscles. In these animals, we observed an increase in flexor burst duration and amplitude when hip flexion was blocked despite the inability of the IP muscle to provide any sensory input. Figure 3.6A illustrates averaged filtered and rectified EMG records comparing blocked with undisturbed stepping in a cat with IP tenotomy. In this example, blocking of flexion occurred 132 ms after the onset of the IP burst (denoted by black arrows). In figures 3.6*B* and C, we present grouped data from 3 animals with IP tenotomy (shaded bars) compared with 6 animals without IP tenotomy (white bars) where hip flexion was blocked between 50 and 150 ms after the onset of the IP burst. Even with the IP detached, the response to blocking flexion appeared largely unaffected. The percent changes in flexor and MG burst duration in animals with IP tenotomy was not statistically significant from those seen in cats with the IP intact ($p > 0.10$) (Fig. 3.6*B*). Similarly, the percent increases in flexor burst amplitudes when the IP was detached were also comparable to those seen in cats with the IP intact ($p > 0.10$) (Fig. 3.6C).

Figure 3.6. Effect of IP Tenotomy on the Response to Blocking Hip Flexion.

A. Averaged EMG records of hip flexors from one cat with the ipsilateral IP muscle detached from its insertion. Arrows indicate the onset of blocking hip flexion. *B* and C. Summary of the mean change in IP, SartA, SartM, and MG burst duration (*B*) and IP, SartA, and SartM amplitudes (C). Error bars indicate standard error. White bars represent grouped data from cats without IP tenotomy. Grey bars represent grouped data from cats with IP tenotomy. Only the responses to blocking hip flexion that occurred between 50 and 150 ms after the onset of the IP burst are included.

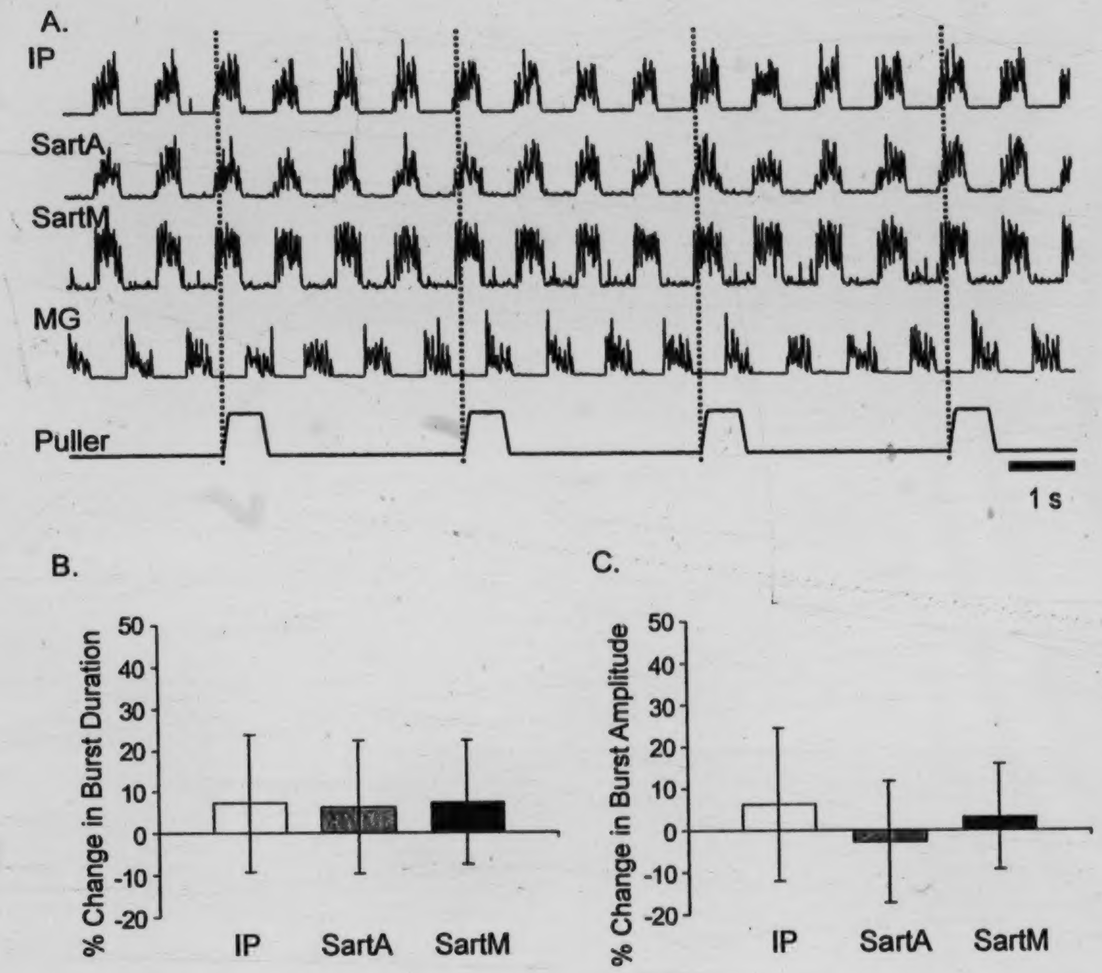

A.
Block
n = 7
IP
Undisturbed
n = 15
SartA
SartM
200 ms
B.
% Change in Burst Duration
40
30
20
10
0
-10
-20
IP
SartA
SartM
MG
C.
☐ IP intact
▨ IP detached
% Change in Burst Amplitude
80
60
40
20
0
IP
SartA
SartM

To further investigate the possible role of muscle afferents from the IP muscle, the tendon of the muscle was detached with a part of its bony insertion intact in 2 animals. The muscle was then tied to a muscle puller (Hiebert et al. 1996). The IP muscle afferents were activated by a stretch via the muscle puller of 5 - 9 mm, 50 ms rise time, and 300 - 500 ms duration. Figure 3.7A illustrates an example of a bout of stepping during which the IP was stretched during flexion (5 mm, 500 ms duration). Averaged data, taken from the same animal whose locomotor activity is partially shown in figure 3.7A, is shown in figure 3.7*B* (n = 100 steps). The average increase in IP burst duration was 7.3 ± 16.6%. SartA burst duration increased by 6.4 ± 16.0% and SartM burst duration increased by 7.4 ± 14.8%. The average increase in IP burst amplitude was 6.1 ± 18.2%. SartA burst amplitude changed by –2.7 ± 14.4% and SartM burst amplitude increased by 3.2 ± 12.6%. The response to stretch of the IP muscle was variable and subtle with a large range of responses and small changes in duration or amplitude, consistent with the finding that IP tenotomy had no effect on the response to blocking hip flexion (Fig. 3.6).

Since IP tenotomy had little effect on the response to blocking flexion and the response to stretch of the isolated IP muscle was negligible, we turned our attention to examining the role of proprioceptive feedback from the sartorius muscles during the swing phase. In one experiment, the SartA and SartM muscles were cut near their distal attachments, leaving the IP as the sole major hip flexor. In this animal, we noticed that the response to blocking forward swing was diminished to those observed in other cats whose SartA and SartM muscles were intact. In subsequent experiments (n = 8), we looped a thread around the SartA and SartM nerves. Following a period of baseline stepping, we tied

Figure 3.7. Response to IP Stretch during Walking.

A. Rectified and filtered EMG records from ipsilateral hip flexors and ankle extensor muscles. Abbreviations are the same as in previous figures. Bottom trace illustrates IP stretch (5 mm, 500 ms duration). *B* and C. The percent change in IP, SartA, and SartM burst duration (*B*) and amplitude (*C*) in response to pulling the IP was small and variable.


A.
IP
SartA
SartM
MG
Puller
1 s
B.
% Change in Burst Duration
50
40
30
20
10
0
-10
-20
IP
SartA
SartM
C.
% Change in Burst Amplitude
50
40
30
20
10
0
-10
-20
IP
SartA
SartM

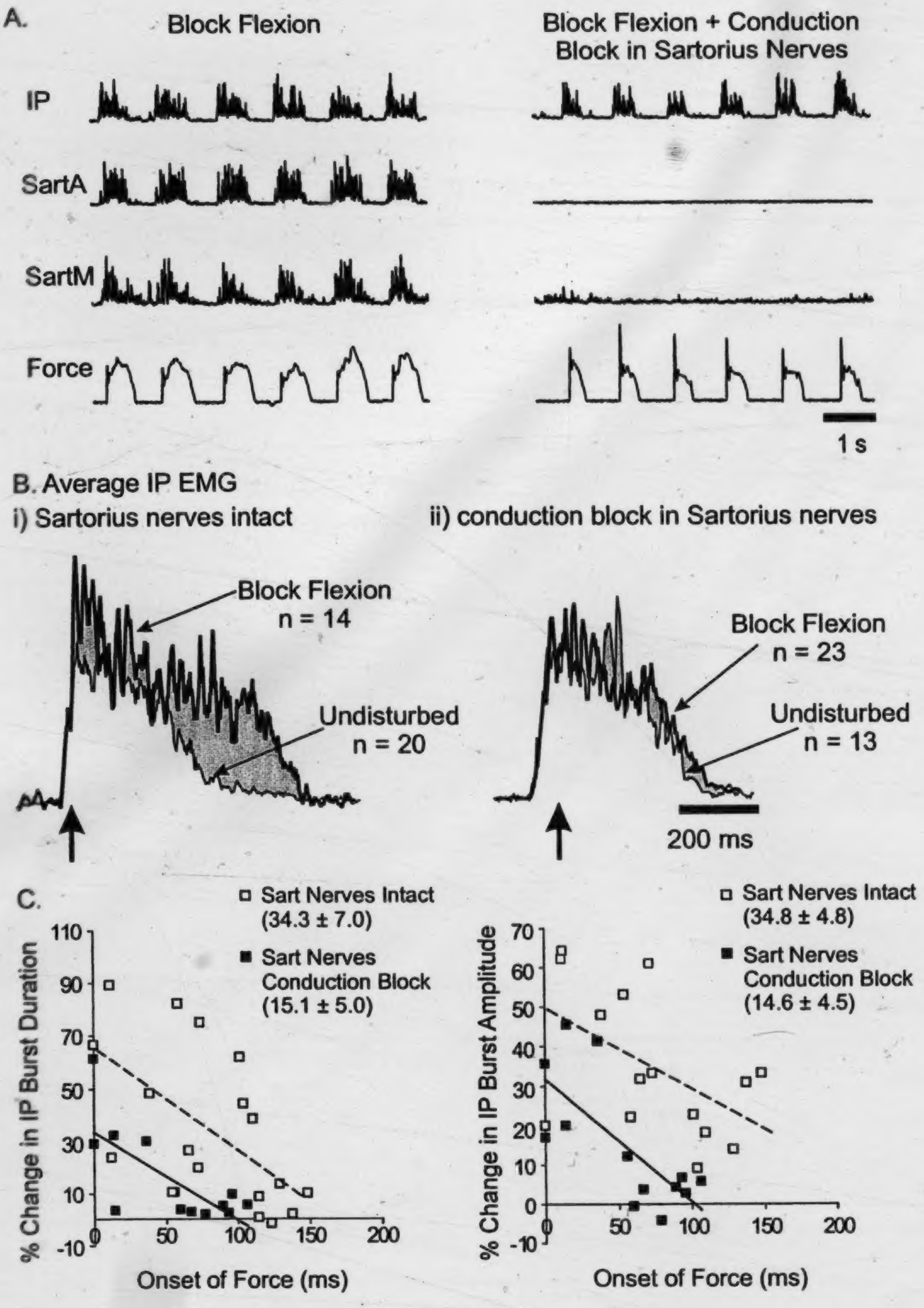
off and pulled on this thread to block conduction in the nerves. We determined that conduction was successfully blocked by the loss of sartorius EMG activity. In 5 animals, we were able to record responses to blocking hip flexion both before and after conduction block in the SartA and SartM nerves. Figure 3.8A illustrates an example of a sequence of stepping during which flexion was blocked in 1 of these animals. Note also the decrease in the level of activity in the IP muscle after conduction block in the sartorius nerves (Fig. 3.8*A*). Figure 3.8*B*(i) shows the characteristic response to blocking flexion in the IP muscle before conduction in the sartorius nerves was blocked (shaded area). Averaged IP EMG records from the same cat are shown in figure 3.8*B*(ii) after conduction in the sartorius nerves was blocked. As illustrated, the response to blocking the limb during flexion was diminished (shaded area). Figure 3.8C shows data from 5 animals demonstrating the general diminished response to blocking. Each point in the scatterplot represents the average IP burst duration and amplitude from a stepping sequence (n = 5 animals, mean ± SE in parentheses). There was a significantly smaller overall response in IP burst duration and amplitude to blocking swing after conduction block in the sartorius nerves ($p < 0.01$).

3.3.3 The Influence of Contralateral Limb Activity on Ipsilateral Flexor Burst Activity

Although we were able to obtain a prolongation of the hip flexor burst when the swinging limb was blocked, we sought to find out what was limiting this prolongation. We reasoned that inhibitory coupling between the flexor generating system in the two limbs would limit the extent to which the flexor bursts could be prolonged (Lundberg 1981). If this is true, then flexor activity in the two hindlimbs should not be observed at the same time. We quantified this idea by comparing the duration of the ipsilateral IP burst with the

Figure 3.8. Effect of Blocking Conduction in the Sartorius Nerves on the Response to Blocking Hip Flexion.

A. Rectified and filtered EMG records from ipsilateral hip flexor muscles. Abbreviations are the same as in previous figures. Note the diminished effect of blocking flexion after the sartorius nerves were pulled. *B.* i) Averaged EMG traces of the IP muscle with sartorius nerves intact. Thick trace represents blocked steps and thin trace represents undisturbed steps. ii) Averaged EMG traces of the IP muscle with conduction blocked in the sartorius nerves. Thick trace represents blocked steps and thin trace represents undisturbed steps. C. Scatterplots comparing the response to blocking the limb before (open squares) and after (filled squares) conduction in sartorius nerves was blocked. Numbers in parentheses represent the mean ± standard error of the percent change in burst duration and amplitude across all animals. The percent change in IP burst duration and amplitude was lower after conduction in the sartorius nerves was blocked compared to control ($p < 0.01$).

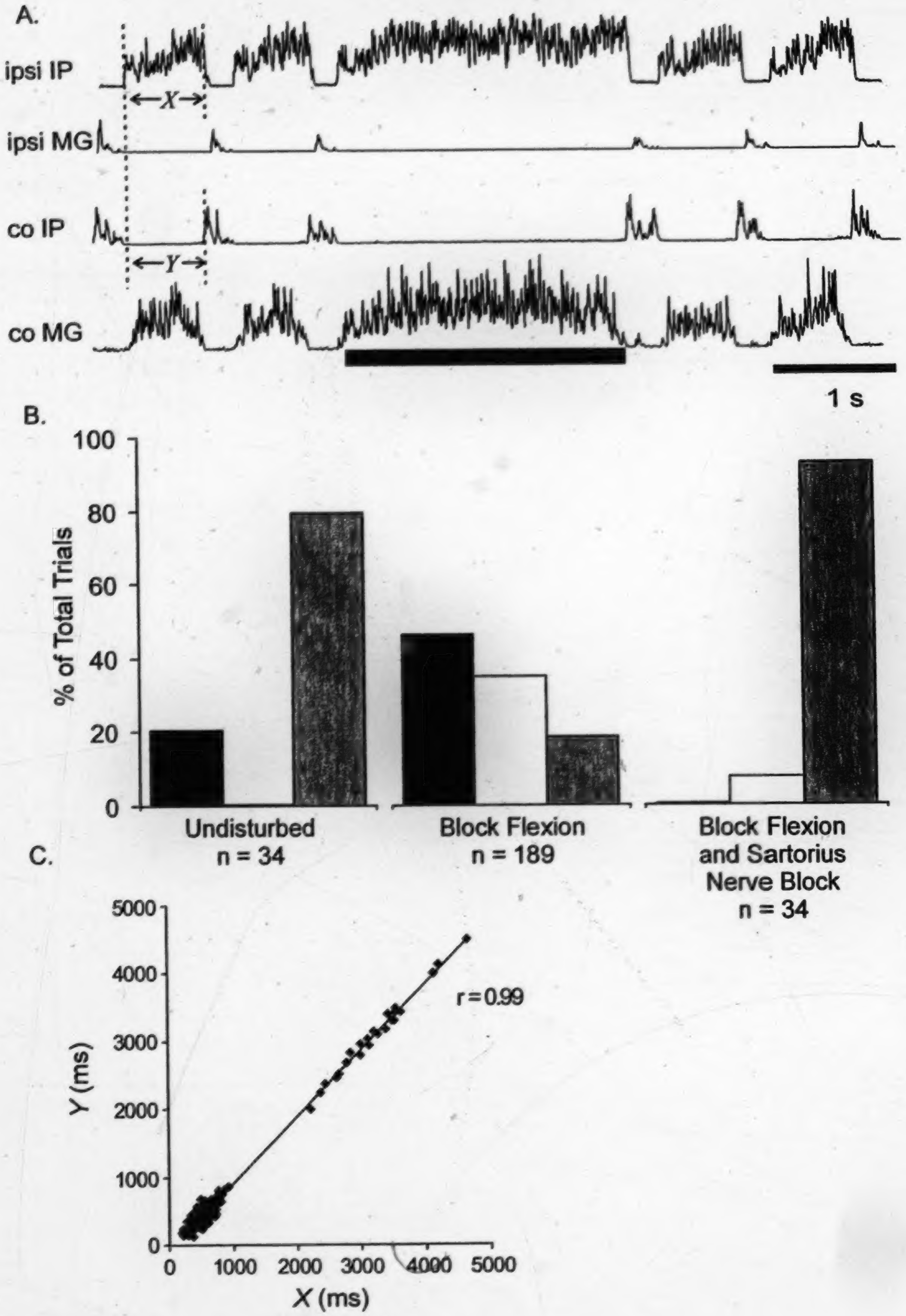

A.
Block Flexion
Block Flexion + Conduction Block in Sartorius Nerves
IP
SartA
SartM
Force
1 s
B. Average IP EMG
i) Sartorius nerves intact
ii) conduction block in Sartorius nerves
Block Flexion n = 14
Undisturbed n = 20
Block Flexion n = 23
Undisturbed n = 13
200 ms
C.
□ Sart Nerves Intact (34.3 ± 7.0)
■ Sart Nerves Conduction Block (15.1 ± 5.0)
% Change in IP Burst Duration
110
90
70
50
30
10
-10
0
50
100
150
200
Onset of Force (ms)
□ Sart Nerves Intact (34.8 ± 4.8)
■ Sart Nerves Conduction Block (14.6 ± 4.5)
% Change in IP Burst Amplitude
70
60
50
40
30
20
10
0
-10
0
50
100
150
200
Onset of Force (ms)

interval between the onset of ipsilateral IP activity and the onset of contralateral IP activity. These values are indicated as Y and X, respectively, in figure 3.9A. If the flexor half-centres are mutually inhibitory, then the values of X and Y should be correlated. Y should not be much greater than X although the reverse is possible: the duration of the ipsilateral IP burst (Y) can be much shorter than the interval to the onset to the next contralateral IP burst (X). To test this idea, we attempted to lengthen the interval X by delaying the onset of the burst in the contralateral hip flexors by briefly stopping the treadmill during mid-stance of the contralateral limb (Fig. 3.9A). When this was done, the duration of the ipsilateral IP burst was prolonged for the duration of the delay to the onset of the contralateral flexor burst in 21% of the trials (Fig. 3.9*B*, *Undisturbed*, black bar). In the remainder of the trials, we observed either a cessation of the locomotor rhythm or a continuation of ipsilateral stepping with no change to the duration of the IP bursts (represented by grey bars in Fig. 3.9*B*).

The combination of blocking hip flexion and delaying the onset of contralateral swing resulted in prolongation of ipsilateral IP burst activity in 82% of the trials (Fig. 3.9*B*, *Block Flexion*, black and white bars). In 57% of these trials (black bar), the duration of the IP burst was extended for the duration of the delay to the onset of the contralateral flexor burst. In the remaining 43% of these trials (white bar), the duration of the IP burst was, on average, prolonged by 63% (and at least by 12%) compared to the preceding IP burst (white bar) but terminated at least 10 ms before the resumption of contralateral flexor activity. In the remaining 18% of the trials, we observed either continuation of alternating bursts between ipsilateral flexors and extensors or cessation of ipsilateral flexor activity (grey bar).

Figure 3.9. The Effect of Delaying the Onset of Contralateral Flexor Activity.

A. Prolongation of flexor burst duration by delaying the onset of the contralateral flexor burst. Stopping the treadmill briefly (thick black line) inhibited contralateral flexor activity and resulted in the prolongation of ipsilateral flexor activity. *B*. The occurrence of the response illustrated in A to inhibiting contralateral flexor activity under three situations (Undisturbed, Block Flexion, Block Flexion and Sartorius Nerve Block). Black bars represent the incidence of observing a prolongation of IP burst duration for the duration of the delay to the onset of the contralateral flexor burst (exemplified in *A*). White bars represent the incidence of observing a prolongation of IP burst duration, but not for the extent of time that contralateral flexor burst onset was delayed. Grey bars represent the incidence of observing other responses. These other responses consisted of either no effect on flexor burst duration with continuation of ipsilateral stepping or cessation of stepping rhythm. Note that although prolongation of flexor activity was occasionally observed even after conduction in the sartorius nerves was blocked, the prolongation never continued for as long as the inhibition was applied (i.e. for as long as the treadmill was stopped). Sample size (n) refers to the number of trials recorded under each situation from 6 animals. C. If flexor half-centres are mutually inhibitory, then the duration of the ipsilateral IP burst (denoted by Y in A) should coincide with the interval between the onset of ipsilateral IP activity and the onset of contralateral IP activity (denoted by X in *A*). Data in the scatterplot represents values measured from one cat. The relationship between X and Y was almost perfectly correlated ($r = 0.99, p < 0.05$).


A.
ipsi IP
←X→
ipsi MG
co IP
←Y→
co MG
1 s
B.
100
80
60
40
20
0
% of Total Trials
Undisturbed
n = 34
Block Flexion
n = 189
Block Flexion
and Sartorius
Nerve Block
n = 34
C.
5000
4000
3000
2000
1000
0
Y (ms)
r = 0.99
0
1000
2000
3000
4000
5000
X (ms)

If conduction in the sartorius nerves was blocked, the dominant response was either a cessation of locomotor rhythm or a continuation of ipsilateral stepping with no change in the duration of the IP bursts compared to the preceding step (represented by grey bar in Fig. 3.9B, *Block Flexion and Sartorius Nerve Block*). Prolongation of ipsilateral IP bursts was rarely observed (8% of the trials) (white bar). Even when prolongation was observed, it never lasted for the duration of the delay to the onset of the contralateral flexor burst.

The example shown in figure 3.9A represents the upper limit of the relationship between ipsilateral IP burst duration (Y) and the interval between the onsets of the ipsilateral IP and the subsequent contralateral IP (X). If the flexor half centers on both sides inhibit each other, then the greatest extension of ipsilateral flexor activity should coincide with the duration of time that the onset of contralateral flexor activity is delayed (exemplified in Fig. 3.9A). Indeed, we found that for all animals tested, the relationship between X and Y was strongly correlated. In figure 3.9C, the values X and Y from steps taken from 1 cat (n = 489 steps) are plotted. Data points that are located at the top right of the plot are those measured from the trials where the onset of contralateral swing was briefly inhibited and hip flexion was blocked. Data points that are clustered close to the bottom corner of the plot (where X is less than 2000 ms) are those measured from sequences of undisturbed stepping and those during which hip flexion was blocked. The relationship between X and Y was significantly correlated ($r = 0.99$, $p < 0.05$).

3.4 Discussion

The purpose of this investigation was to determine whether modification of afferent feedback from hip flexor muscles influences the burst activity in these muscles during the swing phase of stepping in decerebrate walking cats. Modifying afferent feedback with natural perturbations to the contracting muscles was found to strongly influence the duration and amplitude of bursts in these muscles. Assisting hip flexion movements decreased flexor burst activity (Fig. 3.2), while resisting hip flexion enhanced flexor burst activity (Fig. 3.3 and 3.5). These effects occur in the absence of sensory input from the skin and other leg muscles, and they depend largely on modification of feedback from the sartorius muscles (Fig. 3.8). Furthermore, sensory feedback from the sartorius muscle was capable of maintaining flexor burst activity for long periods when stepping in the contralateral leg was inhibited at the same time that ipsilateral hip flexion was resisted (Fig. 3.9).

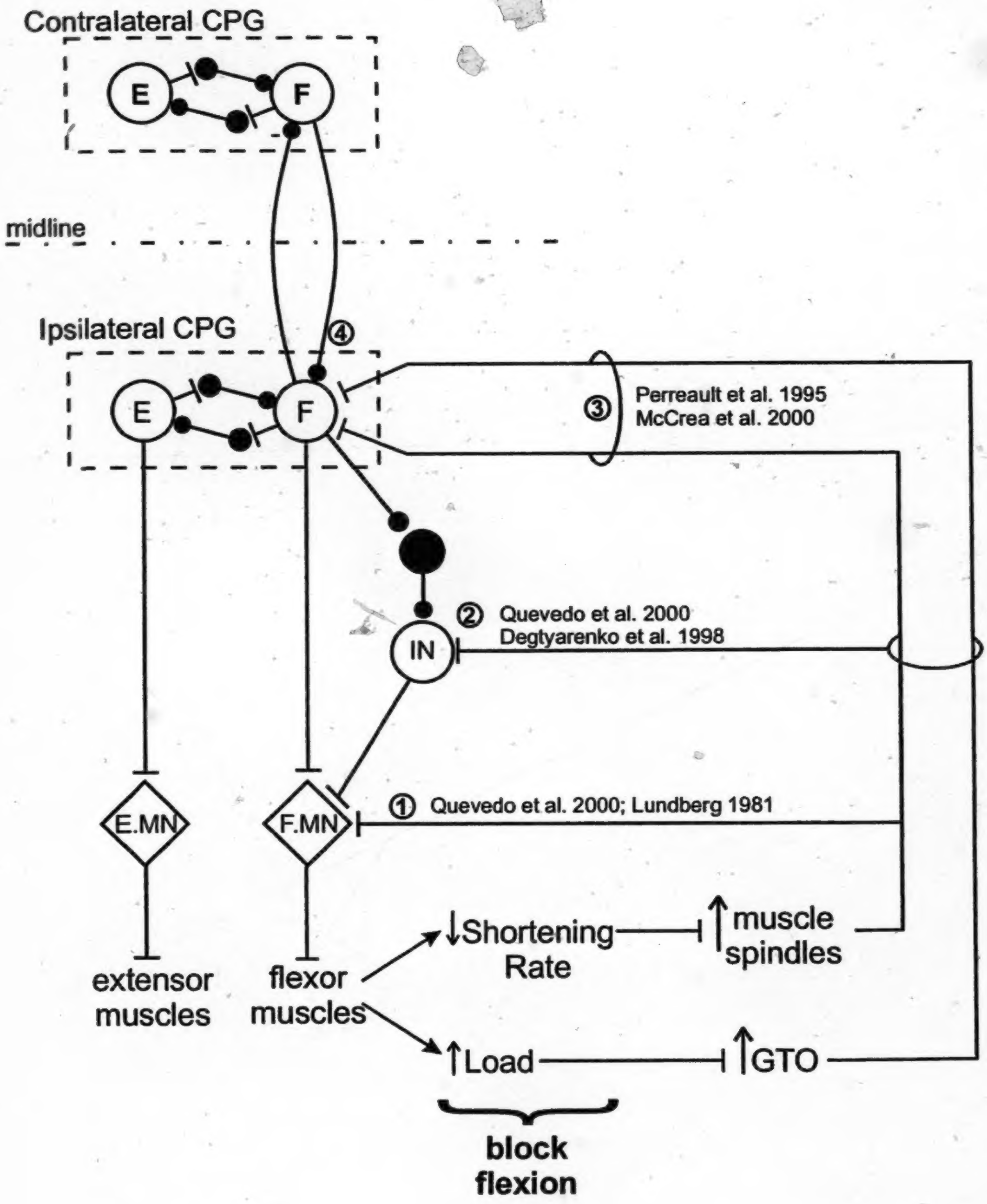
3.4.1 Modulation of Flexor Activity by Flexor Muscle Afferents during the Swing Phase

Based on previous findings and the results from this investigation, a scheme for explaining the role of afferent feedback during the swing phase of walking is shown in figure 3.10. This scheme bears a close resemblance to the pathways by which extensor group I muscle afferent input can enhance extensor activity during the stance phase (reviewed in Pearson 1995). Assuming that the CPG for each leg consists of flexor and extensor half-centers that mutually inhibit each other (Lundberg 1981), input from group I afferents from hip flexor muscles could enhance activity in flexor motoneurons via monosynaptic and disynaptic pathways (Lundberg 1981; Degtyarenko et al. 1998; Quevedo et al. 2000) and via the locomotor CPG (Perreault et al. 1995; McCrea et al. 2000).

The monosynaptic excitatory pathway from flexor group I afferents to flexor motoneurons is represented as *pathway 1* in figure 3.10. In addition to homonymous

Figure 3.10. Schematic Diagram of Hypothesized Afferent Pathways from Flexor Muscles that Enhance Flexor Activity.

Black dots represent inhibitory connections while bars represent excitatory connections. E and F, extensor and flexor half-centers, respectively. E.MN and F.MN, extensor and flexor motoneurons, respectively. IN, interneuron. For simplicity, the afferent connections of the extensor system are not shown. Three pathways are involved in enhancing flexor activity (references indicated in diagram). *Pathway 1*: an excitatory monosynaptic pathway from group I afferents. *Pathway 2*: disynaptic group I pathways from flexor afferents that are disinhibited by the CPG. *Pathway 3*: a direct pathway from flexor group I afferents to the locomotor CPG. Activation of *pathways 1, 2,* and 3 could account for our observation of enhanced flexor activity when hip flexion is blocked. In addition, ipsilateral flexor burst activity is limited by activity on the contralateral side (*pathway 4*). See text for further details.


Contralateral CPG
E
F
midline
Ipsilateral CPG
④
E
F
③
Perreault et al. 1995
McCrea et al. 2000
②
Quevedo et al. 2000
Degtyarenko et al. 1998
IN
①
Quevedo et al. 2000; Lundberg 1981
E.MN
F.MN
↓Shortening Rate
↑muscle spindles
extensor muscles
flexor muscles
↑Load
↑GTO
block flexion

monosynaptic connections, heteronymous connections exist between flexor group I afferents and flexor motoneurons. For example, the excitatory connection from Ia sartorius afferents to IP motoneurons (Eccles and Lundberg 1958) was proposed by Lundberg (1981) to influence IP activity during the swing phase of walking. Very recently, Quevedo et al. (2000) demonstrated that monosynaptic excitation of TA motoneurons could be elicited via heteronymous as well as homonymous flexor group I afferent connections during fictive locomotion in decerebrate cats.

Disynaptic excitatory pathways from flexor group I afferents to flexor motoneurons are represented as *pathway 2* in figure 3.10. Evidence for these pathways comes from recent studies of fictive locomotion in decerebrate cats (Degtyarenko et al. 1998; Quevedo et al. 2000). At rest there is little disynaptic excitation of flexor motoneurons from flexor group I afferents (Quevedo et al. 2000). However, during the flexion phase of locomotor activity, excitatory transmission is powerfully enhanced in homonymous and heteronymous group I disynaptic pathways to flexor motoneurons of the hip, knee, ankle, and bifunctional muscles, including sartorius (Quevedo et al. 2000). Degtyarenko et al. (1998) also provide evidence for excitatory disynaptic reflex pathways from EDL and TA group I afferents to their respective motoneurons during the flexion phase of fictive locomotion in cats.

Lastly, evidence for group I afferent input from flexor muscles to the locomotor CPG comes from the work of Perreault et al. (1995) and McCrea et al. (2000). They reported that stimulation of group I afferents from the iliopsoas and sartorius muscles enhances and prolongs flexor activity with a concomitant increase in step cycle duration during fictive locomotion in decerebrate cats. The direct pathway from group I muscle afferents to flexor motoneurons via the flexor half-center is indicated by *pathway* 3 in figure 3.10.

Based on these previous findings, the scheme illustrated in figure 3.10 can account for our results as follows. Blocking (resisting) hip flexion causes the hip flexors to shorten more slowly than normal, thus resulting in increased spindle and Golgi tendon organ activation from these muscles. While activity patterns in group Ib afferents from flexor muscles during swing has not been reported to date, spindle afferents from the sartorius muscles have been shown to be active during the swing phase in walking cats (Loeb et al. 1985; Loeb and Hoffer 1985). With the slower shortening of the flexor muscles, the expected reduction in group I activity near the end of swing would not occur, and excitatory drive onto the flexor motoneurons would be increased via one or possibly all of the pathways indicated by previous studies (Lundberg 1981; Perreault et al. 1995; Degtyarenko et al. 1998; Quevedo et al. 2000). Enhanced activation in the pathways onto the flexor half-center would lead to prolonged burst activity. The opposite effects would occur when hip flexion is assisted. In this situation, the hip flexors would shorten and unload more rapidly, thus prematurely reducing the excitatory group I input to the flexor motoneurons and resulting in an abbreviation of activity in the flexor half-center and therefore reduce flexor burst duration.

The extent to which afferents other than the group I afferents might be involved in producing the effects we have observed is difficult to assess. For example, there is no clear consensus on the action of group II flexor muscle afferents on flexor activity during swing. During fictive locomotion, McCrea et al. (2000) reported that stimulation of afferents from the iliopsoas and sartorius muscles at group II strengths can enhance flexor activity, whereas Perreault et al. (1995) reported that stimulation of group II afferents in the sartorius nerve resets the locomotor rhythm to extension. In walking decerebrate cats, stimulation of the EDL nerve at group II strengths produces an increase in the duration of the IP burst while stimulation of the TA nerve (at group II strengths) produced either no effect or an excitatory effect on flexor burst duration (Hiebert et al. 1996). Another source of excitatory input to the flexor burst generating system is the non-spindle group II afferents and smaller afferents. These afferents form a major component of the 'flexor-reflex afferents' (Burke 1999) so if they were activated with the contracting hip flexors they may have contributed to facilitating flexor burst activity when hip flexion was resisted or blocked. Another possible source of afferent input is from the hip joint. However, the effects of blocking hip flexion were significantly weakened following conduction block in the sartorius nerve (Fig. 3.9*B*). This procedure would not have influenced hip joint afferents. Thus, we believe that hip joint afferents do not contribute substantial afferent input to hip flexor muscle activity during swing. It is conceivable, however, that some of the residual effect of blocking hip flexion, in the absence of feedback from sartorius muscles, is due to input from hip-joint afferents.

The usual criterion for establishing whether a specific input has an effect on the CPG is examining whether or not the locomotor rhythm has been reset by the disturbance in question (Hultborn et al. 1998). Given the nature of treadmill stepping and the type of perturbations used, we cannot use this criterion to test that the perturbations we used influence the locomotor CPG. However, 2 lines of evidence are consistent with the proposal that our proprioceptive disturbances to hip flexor activity (i.e. assisting and resisting/blocking flexion) are accessing the CPG. First, when we blocked hip flexion we observed prolongation of flexor activity accompanied by a decrease in the subsequent ipsilateral extensor burst duration (Fig. 3.5 and 3.6). Step cycle duration was not significantly affected by the perturbation; however, effects on cycle duration would not be obvious because the speed of the treadmill entrains the locomotor rhythm via the stepping legs. Second, the duration of the flexor bursts could be greatly enhanced by the addition of proprioceptive feedback and this enhancement is further reinforced when stepping in the contralateral leg is stopped. We propose that flexor burst activity, although enhanced, is not maintained for a long period when flexion is resisted or blocked because the bursts are terminated by inhibitory input from the contralateral flexor burst generator (Lundberg 1981) (*pathway* 4 in Fig. 3.10). Indeed, flexor activity from both sides strongly alternate with each other (Fig. 3.9C). When the onset of the contralateral flexor burst was delayed, prolongation of ipsilateral flexor activity for seconds could easily occur when hip flexion was blocked (Fig. 3.9A and B, middle histogram). Without this additional proprioceptive input, prolongation of ipsilateral flexor activity occurred only 21% of the time (Fig. 3.9B, left histogram).

3.4.2 Feedback from the Sartorius Muscles is Important for Enhancing Flexor Burst Activity

We have been able to show a difference in the importance of afferent feedback from the IP and sartorius muscles during the swing phase. When the IP muscle was detached from its insertion, we saw little change in the response to blocking swing. This was consistent with the small effects produced by stretching the IP muscle (Fig. 3.7). Given these results, we conclude that afferent feedback from the IP muscle has a small role in the modulation of flexor burst activity. Conversely, we found that when conduction in the sartorius nerves was interrupted, the enhancement in hip flexor activity when hip flexion was blocked was not present (Fig. 3.8). Furthermore, activity in the IP muscle was reduced even during undisturbed stepping after conduction block in the sartorius nerves (Fig. 3.8A). The heterogeneity among individual muscles' roles in the modulation of flexor burst activity extends previous findings from decerebrate walking cats. The IP, TA, and EDL muscles have been previously reported to yield different effects on flexor burst activity when their afferents have been activated (Hiebert et al. 1996). Furthermore, given the different anatomical features of the IP and sartorius muscles (see Fig. 3.1C), it is not surprising that they would each have a unique contribution to the modulation of flexor burst activity.

3.4.3 Functional Relevance

The scheme proposed in figure 3.10 could provide for appropriate pathways by which effective flexor activity can be produced despite perturbations to limb motion. For example, this may provide a mechanism for appropriate modifications to the locomotor pattern when animals walk along inclined surfaces during which there is an increase in flexor burst activity during swing (Carlson-Kuhta et al. 1998). Because the leg has to be lifted more against gravity, there is a tendency to reduce the rate of shortening thus increasing spindle and tendon organ activity above that generated when walking along a horizontal surface. These enhanced afferent signals would then enhance flexor burst activity to accommodate the increased loading of the flexor muscles via the pathways illustrated in figure 3.10. Consistent with this proposal are our unpublished observations that adding a load to the hindlimb of a conscious walking cat (by strapping a weight around the shank) enhances flexor burst activity analogous to that observed in this study.

3.5 References

Burke RE. The use of state-dependent modulation of spinal reflexes as a tool to investigate the organization of spinal interneurons. *Experimental Brain Research* 128:263-77, 1999.

Carlson-Kuhta P, Trank T, Smith JL. Forms of forward quadrupedal locomotion. II. A comparison of posture, hindlimb kinematics, and motor patterns for upslope and level walking. *Journal of Neurophysiology* 79: 1687-1701, 1998.

Degtyarenko AM, Simon ES, Norden-Krichmar T, Burke RE. Modulation of oligosynaptic cutaneous and muscle afferent reflex pathways during fictive locomotion and scratching in the cat. *Journal of Neurophysiology* 79: 447-463, 1998.

Duysens J, Pearson KG. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Research* 187: 321-332, 1980.

Duysens J, Clarac F, Cruse H. Load-regulating mechanisms in gait and posture: comparative aspects. *Physiological Reviews* 1: 83-133, 2000.

Eccles RM, Lundberg A. Integrative pattern of Ia synaptic actions on motoneurones of hip and knee muscles. *Journal of Physiology* 144: 271-298, 1958.

Hiebert GW, Whelan PJ, Prochazka A, Pearson KG. Contribution of hind limb flexor muscle afferents to the timing of phase transitions in the cat step cycle. *Journal of Neurophysiology* 75: 1126-1137, 1996.

Hultborn H, Conway BA, Gossard J-P, Brownstone R, Fedirchuk B, Schomburg ED, Enríquez-Denton M, Perreault M-C. How do we approach the locomotor network in the mammalian spinal cord? *Annals of the New York Academy of Sciences* 860: 70-82, 1998.

Lamb T, Pearson KG. Afferent regulation of the swing phase of locomotion. *Society for Neuroscience Abstracts* 26: 1232, 2000.

Loeb GE, Hoffer JA, Pratt CA. Activity of spindle afferents from cat anterior thigh muscles. I. Identification and patterns during normal locomotion. *Journal of Neurophysiology* 54: 549-564, 1985.

Loeb GE, Hoffer JA. Activity of spindle afferents from cat anterior thigh muscles. II. Effects of fusimotor blockade. *Journal of Neurophysiology* 54: 565-577, 1985.

Lundberg A. Half-centres revisited. In: *Regulatory Functions of the CNS. Motion and Organization Principles, vol.1 Advances in Physiological Sciences*, edited by J Szentagothai, M Palkovits and J Hamori. Budapest: Pergamon Press, 1981, pp. 155-167.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233, 2000.

Orlovskii GN, Shik ML. Standard elements of cyclic movement. *Biophysics* 10: 935-944, 1965.

Orlovsky GN, Deliagina TG, Grillner S. *Neuronal control of locomotion: from mollusc to man.* New York: Oxford University Press, 1999.

Pearson KG. Proprioceptive regulation of locomotion. *Current Opinion in Neurobiology* 5: 786-791, 1995.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Rossignol S. Neural control of stereotypic limb movements. In: *Handbook of Physiology, Section 12: Exercise : Regulation and Integration of Multiple Systems,* edited by LB Rowell and JT Shepherd. New York, NY: American Physiological Society by Oxford University Press, 1996, pp. 173-216.

Shik ML, Severin FV, Orlovskii GN. Control of walking and running by means of electrical stimulation of the mid-brain. *Biophysics* 11: 756-765, 1966.

Whelan PJ, Hiebert GW, Pearson KG. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Experimental Brain Research* 103: 20-30, 1995.

CHAPTER 4

SARTORIUS MUSCLE AFFERENTS INFLUENCE THE AMPLITUDE AND TIMING OF FLEXOR ACTIVITY IN WALKING DECEREBRATE CATS

Adapted from an original manuscript
T. Lam and K. G. Pearson
Experimental Brain Research (In Press)

4.1 Introduction

In order for locomotion to be adaptable to external conditions, the nervous system must receive and appropriately respond to sensory input. One important source of sensory input during locomotion comes from muscle afferents. For example, the level of extensor activity required to support the body during the stance phase of walking is dependent on afferent feedback from extensor muscles (Hiebert et al. 1994; Hiebert and Pearson 1999; Stein et al. 2000). The timing of the locomotor pattern is also highly sensitive to sensory input from muscle afferents. Sensory inputs from both load-sensitive (Conway et al. 1987; Pearson et al. 1992) and length-sensitive afferents (Andersson and Grillner 1983; Kriellaars et al. 1994) strongly entrain the locomotor rhythm. Inputs from length-sensitive hip flexor muscle afferents (Hiebert et al. 1996), as well as load-sensitive afferents from extensor muscles (Duysens and Pearson 1980; Whelan et al. 1995) are important signals for promoting the transition from the stance to the swing phase of walking.

Evidence for the regulation of flexor activity during locomotion by proprioceptive input is beginning to accumulate. A few studies have shown that swing phase activity during locomotion can be influenced by mechanically altering proprioceptive input (Orlovskii and Shik 1965; Lam and Pearson 2001a). Although the specific muscle receptors involved in mediating these effects have not been directly identified, muscle spindles and Golgi tendon organs are likely candidates since there is substantial evidence that large-diameter flexor muscle afferents can modify the locomotor pattern during fictive locomotion in decerebrate cats. Electrical stimulation of the tibialis anterior, extensor digitorum longus, iliopsoas, sartorius, or posterior biceps/semitendinosus nerves at group I strengths during the flexion phase produces prolongation of flexor burst activity (Perreault et al. 1995; McCrea et al. 2000). Stimulation of group I muscle afferents from the iliopsoas and sartorius muscles also increases the magnitude of flexor bursts during the flexion phase (McCrea et al. 2000). The regulation of flexor activity during locomotion by group I flexor muscle afferents could be mediated by monosynaptic or disynaptic excitatory pathways (Degtyarenko et al. 1998; Quevedo et al. 2000) or by pathways that directly influence the locomotor CPG (Perreault et al. 1995; McCrea et al. 2000).

A role for the secondary endings of muscle spindles in regulating swing phase activity is also suggested by studies that have reported effects of group II flexor muscle afferents on flexor burst activity during fictive locomotion, despite the fact that these investigations have yielded varying conclusions. Initially, Perreault et al. (1995) reported that electrical stimulation of group II flexor muscle afferents from the sartorius, tibialis anterior, and semitendinosus nerves during flexion caused a resetting to extension during fictive locomotion in decerebrate cats. Later results from McCrea et al. (2000) showed that stimulation of these same afferents as well as afferents from other flexor nerves during flexion caused an excitatory effect on flexor activity. The latter observation was consistent with the finding in walking decerebrate cats that stimulation of the tibialis anterior or extensor digitorum longus nerves at group II strengths during the flexor phase resulted in a prolongation of flexion (Hiebert et al. 1996).

Are these feedback pathways from group I and II flexor muscle afferents, identified in fictive locomotor preparations, functional during treadmill walking? We approached this question by examining the effects of electrically stimulating the sartorius nerve during treadmill walking in acute decerebrate cats. Our first objective was to confirm that large afferents from sartorius muscles have an excitatory effect on flexor activity during the swing phase of locomotion, which would be consistent with our previous conclusions (Lam and Pearson 2001a) as well as results from fictive decerebrate cat preparations (Perreault et al. 1995; Degtyarenko et al. 1998; McCrea et al. 2000; Quevedo et al. 2000). Our second objective was to clarify the role of group II flexor muscle afferents in regulating flexor activity during locomotion and to determine whether inhibitory, excitatory, or both inhibitory and excitatory influences exist between these afferents and flexor generating systems in the walking decerebrate cat. We focused on the effects of sartorius nerve stimulation since previous results showed that proprioceptive feedback from the sartorius muscle is particularly important for regulating flexor activity during treadmill locomotion (Lam and Pearson 2001a). Preliminary results from this study have been published in abstract form (Lam and Pearson 2001b).

4.2 Methods

The results in this study were obtained from 3 decerebrate cats during treadmill locomotion. All procedures were approved by the University of Alberta Health Sciences Animal Welfare Committee.

4.2.1 Preparation

Animals were initially anesthetized with halothane. The trachea was then cannulated for the continuous administration of the anesthetic. One carotid artery was ligated and the other cannulated for monitoring the blood pressure. One jugular vein was cannulated for the administration of drugs. Intramuscular fine-wire recording electrodes were sewn into the iliopsoas (IP), tibialis anterior (TA), and medial gastrocnemius (MG) muscles of both hindlimbs. Electrode leads were passed under the skin to a connector located externally on the animal's back. The nerves to the sartorius muscles were then exposed and cut at their entry into the muscle. A cuff electrode was placed around the proximal cut end of the nerve with care taken to include both branches to the medial and anterior heads of the sartorius muscle. A laminectomy was performed to expose the L2/3 segments of the spinal cord. Fine-wire electrodes (Cooner Wire AS632, Cooner Wire Company, Chatsworth, CA) were then positioned between the dura mater and the remaining edge of the vertebrae to monitor cord dorsum potentials.

After these procedures, the animal was fixed in a stereotaxic frame over a treadmill. The animal was then decerebrated by transecting the brainstem at a 50° angle from the anterior edge of the superior colliculus. The anesthesia was discontinued at this time. Spontaneous stepping occurred in response to the moving treadmill belt. Manual stimulation to the perineum was sometimes used to assist stepping.

The sartorius nerves were stimulated at 200 Hz with 500-700 ms trains. The stimulus was triggered to occur 50 ms after the onset of the ipsilateral IP or TA burst and delivered every 3rd or 4th burst. Stimulus strength was measured as a multiple of the threshold strength (*T*) required to evoke the smallest potential measured at the cord dorsum. Group I muscle afferents (including both Ia and Ib fibers) are preferentially activated by stimulation strengths ranging from 1.2 to 1.8 *T* while group II muscle afferents are activated by electrical stimulation strength beginning at 2 to 5 *T* (Jack 1978). We used these guidelines to differentiate between the responses to group I and II muscle afferent fibers from the sartorius nerve.

4.2.2 Data Analysis

The analog data were recorded on tape using a Vetter 4000A PCM machine. Sequences of regular consistent stepping were selected and electromyographic recordings subsequently digitized at 500 Hz (high pass 10 Hz, low pass 30 Hz) and stored on computer using a data acquisition system (Axotape 2.0.2, Axon Instruments). Cord dorsum potentials were digitized at a sampling rate of 10,000 Hz. Custom written computer software programs were used to average and plot EMG traces and to measure burst duration and cycle period. Flexor burst amplitude was measured over a 100 ms period during the plateau phase of the burst profile (which usually began 100 ms after the start of the stimulation, see shaded area in Fig. 1*B*). Cycle duration was defined as the time from the onset of an IP burst to the next IP burst. Student's *t*-tests were used to determine significant differences and the level of significance was set at 0.05.

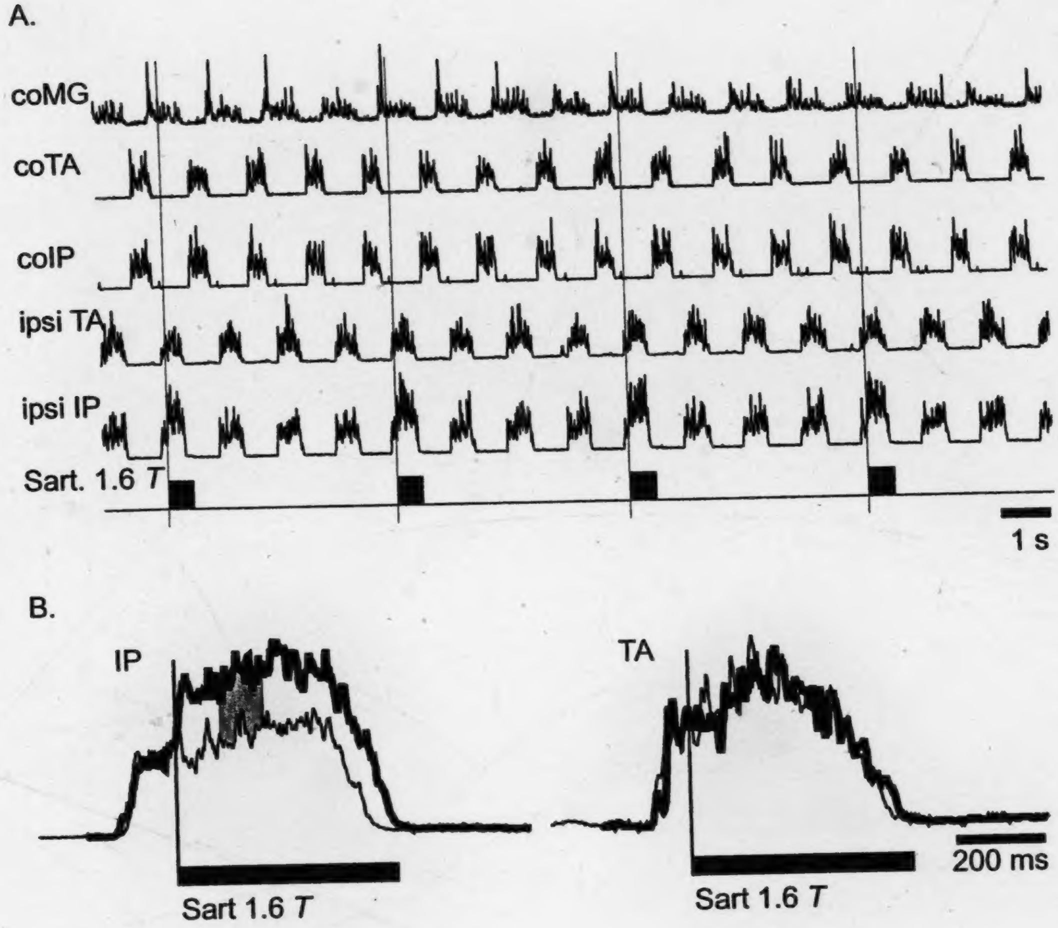
4.3 Results

4.3.1 Effect of Sartorius Group I Afferents on Flexor Burst Duration and Amplitude

Sartorius group I afferents were activated by stimuli of between 1.2 and 1.8 *T* to the sartorius nerve. Figure 4.1A illustrates a sequence of stepping in one animal where stimulation of the sartorius nerve at 1.6 *T* was delivered every fourth step. The increase in IP burst activity (duration and magnitude) is apparent while there was little effect on TA burst activity. Figure 4.1*B* shows averaged EMG bursts of the IP and TA muscles of control steps (thin black line, n = 36 steps), compared with stimulated steps (thick black line, n = 12 steps) from the same sequence of steps that is partly shown in figure 4.1A. In this example, IP burst duration increased by about 10% while TA burst duration increased by

Figure 4.1. The Effect of 1.6 T Sartorius Nerve Stimulation during the Flexor Phase of Locomotion.

A. Stimulation trains of 500 ms at 1.6 T, delivered 50 ms after the onset of the tibialis anterior (TA) burst every 4th step during treadmill locomotion, resulted in an increase in iliopsoas (IP) burst duration and magnitude with no obvious effect on TA burst activity. co, contralateral. ipsi, ipsilateral. B. Averaged EMG records from the IP and TA muscle from the same walking sequence partly shown in A. Shaded area delineates region of the flexor burst from which the change in amplitude was measured. Thick lines represent stimulated IP and TA bursts (n = 12 steps). Thin lines represent averaged IP and TA EMG from control steps (n = 36 steps). The duration of the stimulation train is represented by thick black bar underneath averaged EMG bursts.


A.
coMG
coTA
coIP
ipsi TA
ipsi IP
Sart. 1.6 *T*
1 s
B.
IP
Sart 1.6 *T*
TA
Sart 1.6 *T*
200 ms

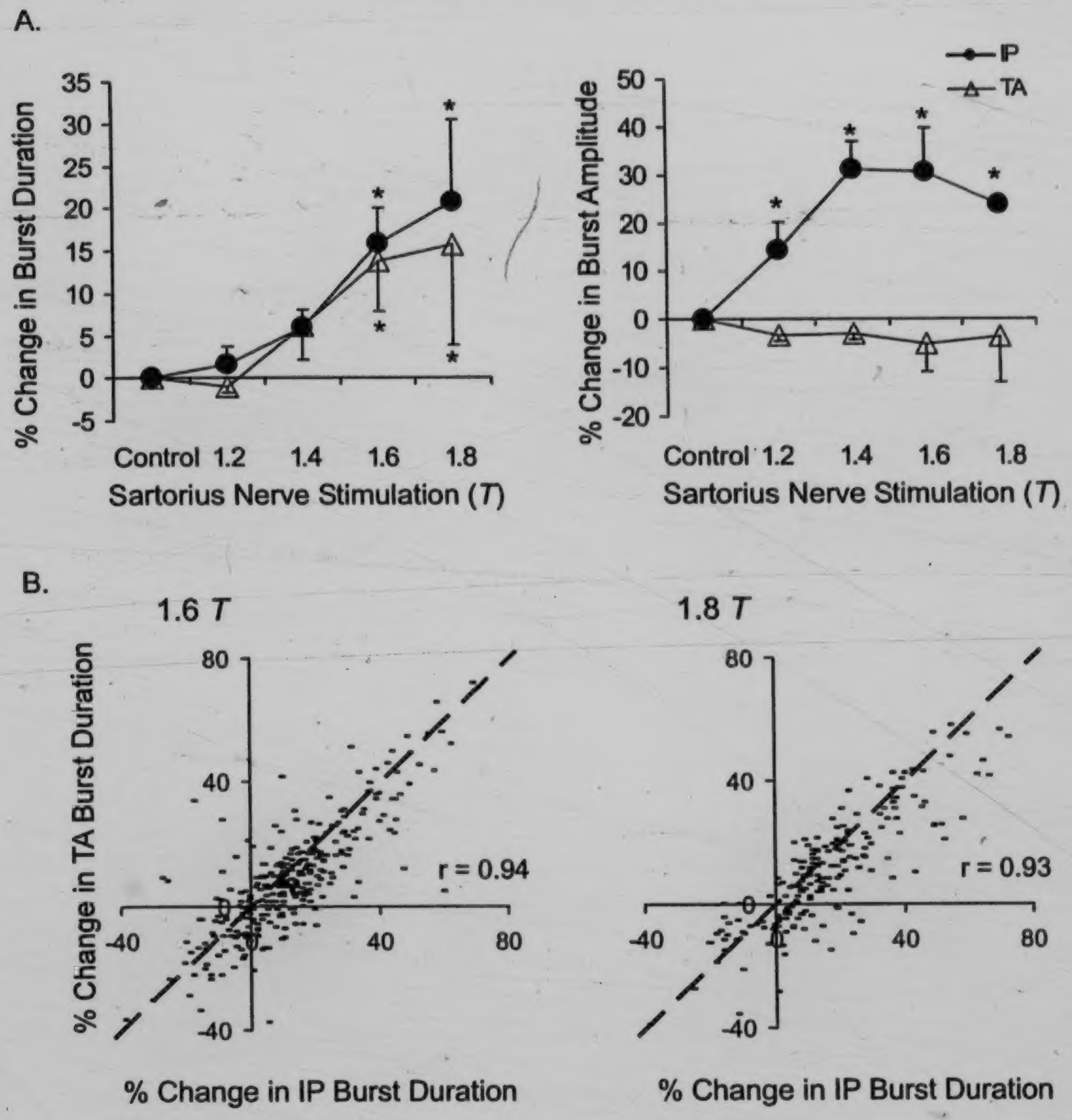
less than 5%. The amplitude of the IP bursts increased by 57% compared to control while the amplitude of the TA was unchanged.

Figure 4.2A illustrates grouped data, from 3 animals, of the percent change in burst duration and amplitude over the range of group I stimulation strengths. As shown in the right panel, stimulation of the sartorius nerve over this range of strengths consistently resulted in an enhancement of IP burst amplitude. The average amplitude was measured over 100 ms beginning 100 ms after the start of the stimulation (see shaded area, Fig. 4.1*B*). The increase in IP amplitude with group I strength stimulation compared to control values was significant across all animals at all strengths tested (1.2 to 1.8 *T*) ($p < 0.05$) (Fig. 4.2A, right panel). TA burst amplitude was largely unchanged but tended to be slightly lower than control with group I sartorius nerve stimulation.

Low threshold stimulation (≤ 1.4 *T*) of sartorius group I afferents did not have a significant effect on IP or TA burst duration. Higher strength stimulation (≥ 1.6 *T*) produced prolongation of both IP and TA burst durations ($p < 0.05$). However, the effects of stimulating the sartorius nerve at 1.8 *T* were more variable. This may be explained by the finding that in one animal, stimulation of the sartorius nerve at 1.8 *T* primarily produced a reduction in IP or TA burst duration, thus yielding mixed results across animals. It is possible that some of the more excitable group II afferents were recruited at this strength in this cat (Jack 1978). Although the increase in TA burst duration was not as large as the increase in IP burst duration measured for a given stimulation strength, there was a strong relationship between the change in IP burst duration and TA burst duration. In figure 4.2*B*, this relationship is shown for stimulation strengths of 1.6 *T* (r = 0.95) and 1.8 *T* (r = 0.93). The dashed line in these figures represents a perfect correlation (r = 1.0) between the

Figure 4.2. The Effect of Sartorius Nerve Stimulation at Group I Strengths on IP and TA Burst Activity.

A. The left panel shows the percent change in iliopsoas (IP) (filled circles) and tibilais anterior (TA) (open triangles) burst duration with a range of group I stimulation strengths. Data from all 3 animals were pooled to generate each data point in the scatterplot. The number of steps represented in the control, 1.2 *T*, 1.4 *T*, 1.6 *T*, and 1.8 T conditions is 843, 54, 107, 453, and 223, respectively. An effect on IP and TA burst duration is only observed with stimulation strengths greater than 1.6 *T*. The right panel shows the percent change in IP and TA burst amplitude. Throughout the range of stimulation strengths, IP burst amplitude was significantly increased with TA burst amplitude remained near or slightly below control. Error bars represent standard error. *, $p < 0.05$. *B*. The relationship between the change in IP burst duration and the change in TA burst duration was quantified for stimulation strengths of 1.6 and 1.8 *T*. The dotted black line in the graphs represents a 1:1 relationship between the change in IP and TA burst duration. Most of the points lay below this line, demonstrating the fact that TA burst duration increased by a lesser degree than IP burst duration with 1.6 or 1.8 *T* sartorius nerve stimulation.


A.
% Change in Burst Duration
35
30
25
20
15
10
5
0
-5
Control
1.2
1.4
1.6
1.8
Sartorius Nerve Stimulation (T)
*
IP
TA
% Change in Burst Amplitude
50
40
30
20
10
0
-10
-20
Control
1.2
1.4
1.6
1.8
Sartorius Nerve Stimulation (T)
B.
1.6 T
1.8 T
% Change in TA Burst Duration
80
40
0
-40
r = 0.94
r = 0.93
% Change in IP Burst Duration
% Change in IP Burst Duration

change in IP and TA burst duration. The majority of the points in the scatterplot are located under this line, reflecting the finding that the increase in TA burst duration, although occurring in conjunction with an increase in IP burst duration, tended to be less.

Although stimulation of the sartorius nerve at $\geq 1.6\ T$ consistently prolonged IP burst duration, the effect on cycle period was modest. Any change in cycle period was measured as a change in the duration between the onsets of successive ipsilateral or contralateral flexor bursts at the time stimulation was delivered and expressed as a percentage of the average control cycle period. Overall, the change in both ipsilateral and contralateral cycle period resulting from group I sartorius afferent stimulation was slight, varying from 0 to 7% and averaging only 2.5% (Fig. 4.3A). However, in a few trials in one animal, stimulation of sartorius group I muscle afferents had a very large effect on cycle period ($p < 0.05$, indicated by asterisks, Fig. 4.3*B*). The prolongation of ipsilateral flexor burst durations in both the IP and TA muscle is apparent, along with a lengthening of the ipsilateral and contralateral cycle period in response to the electrical stimulation. Because these data were outliers compared to the majority of the results, they were not included in the overall averages presented in figure 4.3A.

4.3.2 Effect of Sartorius Group II Afferents on Flexor Burst Duration

An example of a walking sequence during which stimulation of group II sartorius muscle afferents was delivered is shown in figure 4.4. Figure 4.4A illustrates the first 2 stimulus trials of this walking sequence. Initially, 3 *T* stimulation of the sartorius nerve during flexion caused an inhibition of the flexor bursts. Stimulation trains were delivered every 3 steps. Within 5 stimulation trials, this inhibitory effect was gradually replaced by an

Figure 4.3. The Effect of Sartorius Nerve Stimulation at 1.6 and 1.8 T on Locomotor Cycle Period.

A. Typically, there was no effect on locomotor cycle period despite an effect on iliopsoas (IP) and tibilias anterior (TA) burst duration with 1.6 or 1.8 *T* sartorius nerve stimulation. This was a consistent finding from all 3 animals tested (represented by 3 different symbols in the scatterplots). From cat 1, there were 100 steps contributed to the averages in the control condition, 91 steps to the 1.6 *T* condition, and 9 to the 1.8 *T* condition. From cat 2, there were 103 control steps, 56 steps at 1.6 T, and 47 steps at 1.8 T. From cat 3, there were 131 control steps, 97 steps at 1.6 T, and 34 steps at 1.8 T. Error bars represent standard deviations. During some walking sequences in one animal, a strong effect on locomotor cycle period was revealed. An example taken from one of these walking sequences is shown in *B*. These data were not included in the averages illustrated in A. Significant increases in duration are indicated by asterisks ($p < 0.05$). co, contralateral. ipsi, ipsilateral.

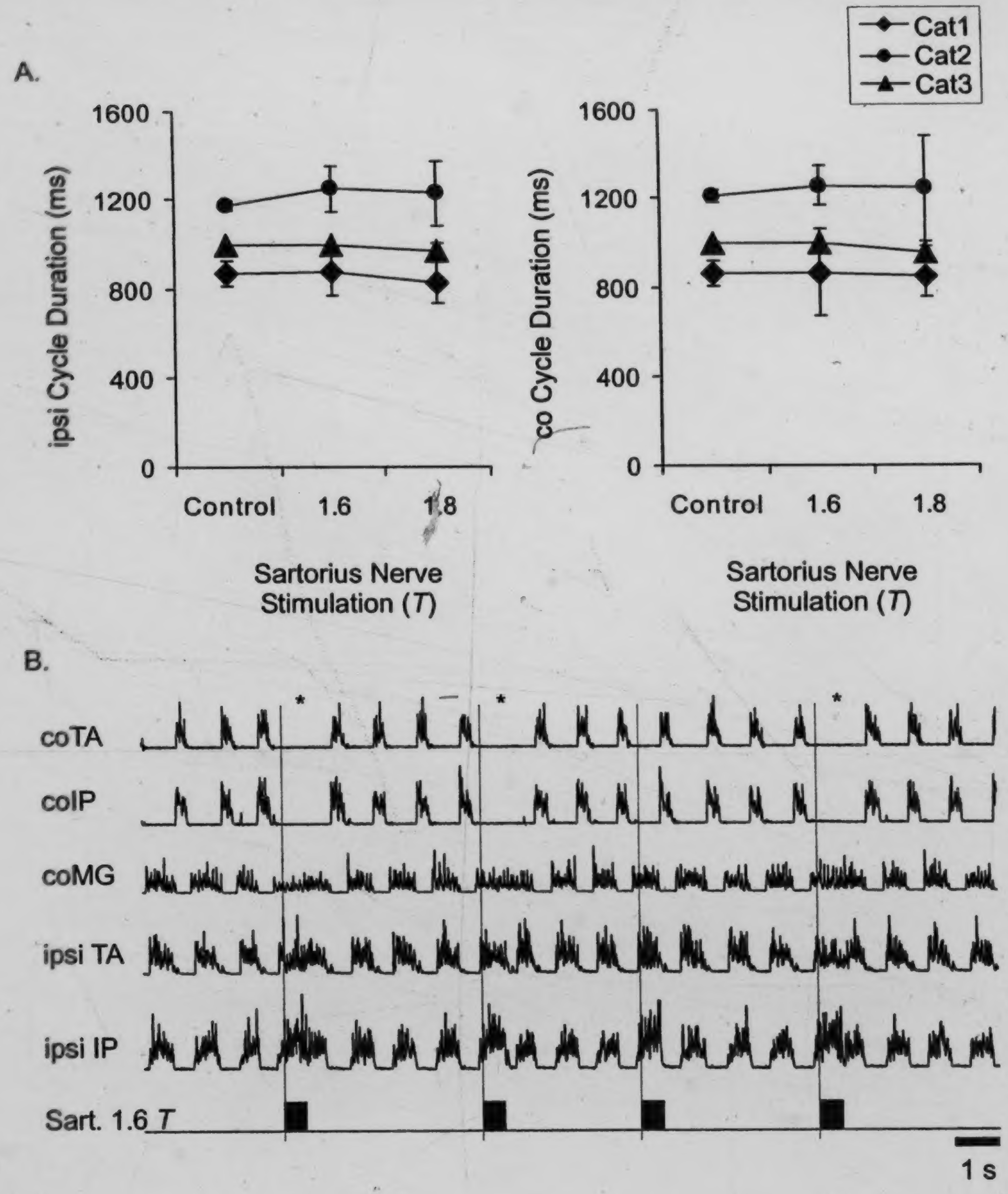
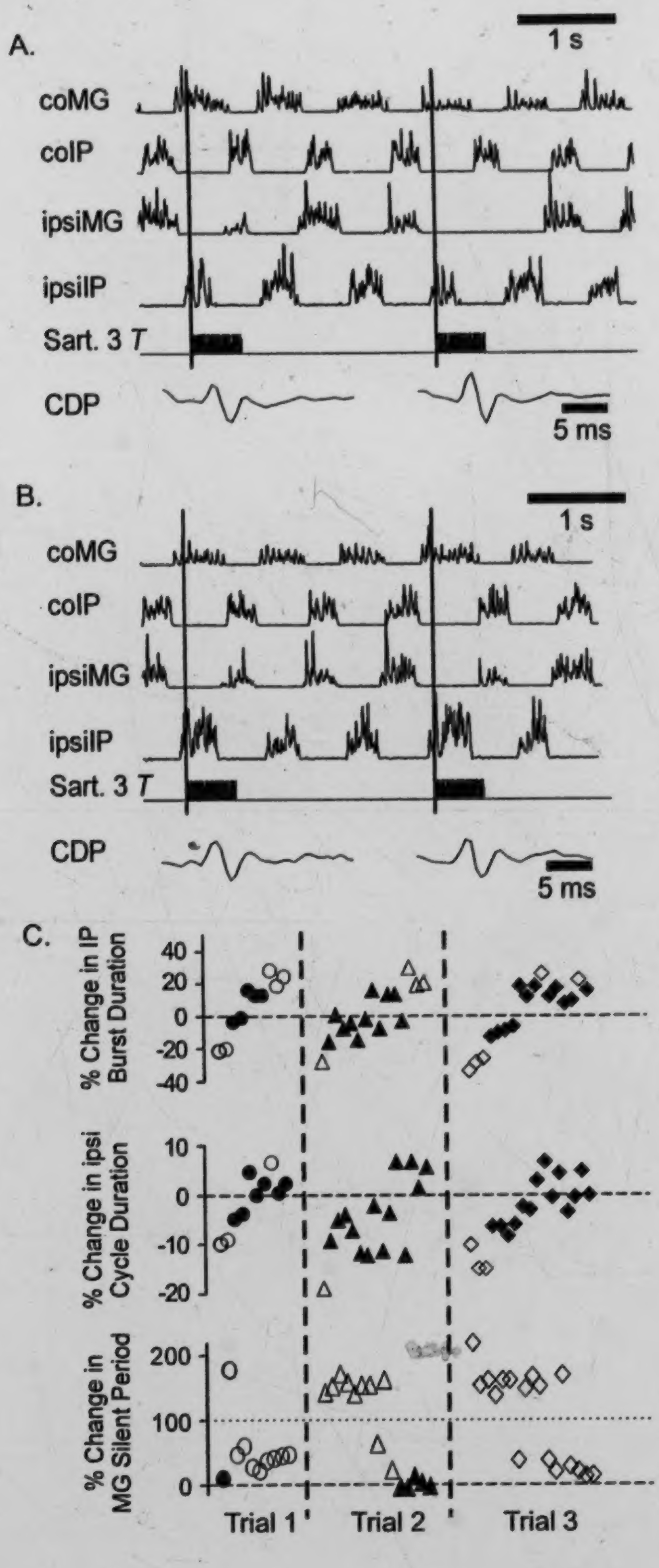

A.
Cat1
Cat2
Cat3
1600
1200
800
400
0
ipsi Cycle Duration (ms)
Control
1.6
1.8
Sartorius Nerve Stimulation (T)
1600
1200
800
400
0
co Cycle Duration (ms)
Control
1.6
1.8
Sartorius Nerve Stimulation (T)
B.
coTA
coIP
coMG
ipsi TA
ipsi IP
Sart. 1.6 T
*
*
*
1 s

Figure 4.4. The Effect of Activating Group II Sartorius Muscle Afferents during the Flexor Phase of Locomotion.

The initial stages (*A*) and the latter stages (*B*) of a single walking sequence during which the sartorius nerve was stimulated at 3 T, 50 ms after the onset of the ipsilateral IP burst. co, contralateral. ipsi, ipsilateral. CDP, cord dorsum potential. There was a gradual reversal from an inhibitory to an excitatory effect on flexor burst activity (C). C. *Top panel,* the percent change in IP burst duration during 3 separate walking trials, each separated by at least 1 minute (delineated by dotted black lines). *Middle panel,* the percent change in cycle duration during the corresponding locomotor sequences. *Bottom panel,* the percent change in the inter-burst interval between MG bursts. Open symbols represent significant ($p < 0.05$) changes in burst or cycle duration compared to control.


A.
1 s
coMG
coIP
ipsiMG
ipsiIP
Sart. 3 T
CDP
5 ms
B.
1 s
coMG
coIP
ipsiMG
ipsiIP
Sart. 3 T
CDP
5 ms
C.
% Change in IP Burst Duration
40
20
0
-20
-40
% Change in ipsi Cycle Duration
10
0
-10
-20
% Change in MG Silent Period
200
100
0
Trial 1
Trial 2
Trial 3

excitatory effect (Fig. 4.4*B*). Figure 4.4*B* illustrates the last 2 stimulus trials of the walking sequence during which 3 *T* stimulation of the sartorius nerve caused an increase in the amplitude and duration of the flexor bursts. Note that the amplitude of the cord dorsum potential (CDP) remained constant throughout the walking sequence. In addition, stimulation of the sartorius nerves at group II strengths also produced an inhibition of the ipsilateral MG burst activity. An example of this is seen in figure 4.4A. This type of response in the ipsilateral MG burst activity was consistent across all animals tested at this stimulation strength.

Figure 4.4C (top panel) quantifies the gradual change in the effect on IP burst duration with activation of group II sartorius muscle afferents for 3 walking sequences, separated by at least 1 minute, including the one illustrated in figures 4.4A and *B*. At the beginning of each trial, 3 *T* stimulation of the sartorius nerve caused a significant decrease in IP burst duration and cycle duration compared to control ($p < 0.05$) (significant responses represented by open symbols) (Fig. 4.4C). Within the walking sequence, however, subsequent 3 *T* stimulation of the sartorius nerve gradually caused a significant increase in IP burst duration ($p < 0.05$) (significant responses represented by open symbols), usually without a corresponding change in cycle duration (Fig. 4.4C, middle panel). To assess the effect on ipsilateral MG activity, the silent period between sequential MG bursts was measured. After 3 *T* stimulation of the sartorius nerve was delivered, the following MG burst was often skipped (indicated by the symbols located above the dotted line, > 100% change in MG silent period). Even if the MG burst was not skipped, its level of activity appeared lower than that of control, as seen in figure 4.4A and *B*.

The pattern of a gradual decrease in the inhibitory effect of group II stimulation on flexor burst activity was observed in 70% of the walking sequences (14/20 walking sequences from 3 cats, stimulation strengths between 3-5 *T* and stimulation trains between 500-700 ms). Variable responses were produced in the remainder of the walking sequences. Persistent inhibitory effects throughout a walking sequence, in response to sartorius nerve stimulation at group II strength, was observed in 3 walking sequences from one cat. In these walking sequences, stimulation of the sartorius nerve was delivered at 4-5 *T* for 500 ms. Stimulation of the sartorius nerve at 3 *T* (500 ms train duration) produced only excitatory effects on IP burst duration during 1 walking sequence. Finally, both inhibitory and excitatory effects on IP burst duration, occurring without a specific time-dependent pattern, were observed in 2 of walking sequences (with 5 *T* sartorius nerve stimulation and 500-700 ms stimulus trains). A summary of the different patterns of responses from the 3 animals is provided in Table 4.1.

Unlike the response to stimulation of the sartorius nerve at group I strength, stimulation of the sartorius nerve at group II strength affected both IP and TA burst duration and amplitude. Figure 4.5A illustrates averaged EMG bursts from the IP and TA muscles at the beginning of a walking sequence (left panel) and from the end of a walking sequence (right panel) during which 5 *T* stimulation of the sartorius nerve was delivered every 4th step. The left panel in figure 4.5A illustrates the inhibitory effect this stimulation had on the initial bursts of the walking sequence. Both the IP and TA muscles showed a decrease in duration and amplitude compared to control steps. At the end of this walking sequence, there was a marked reduction in this inhibitory effect (Fig. 4.5A, right panel). In the IP muscle, there was an emergence to an overall excitatory effect while in the TA

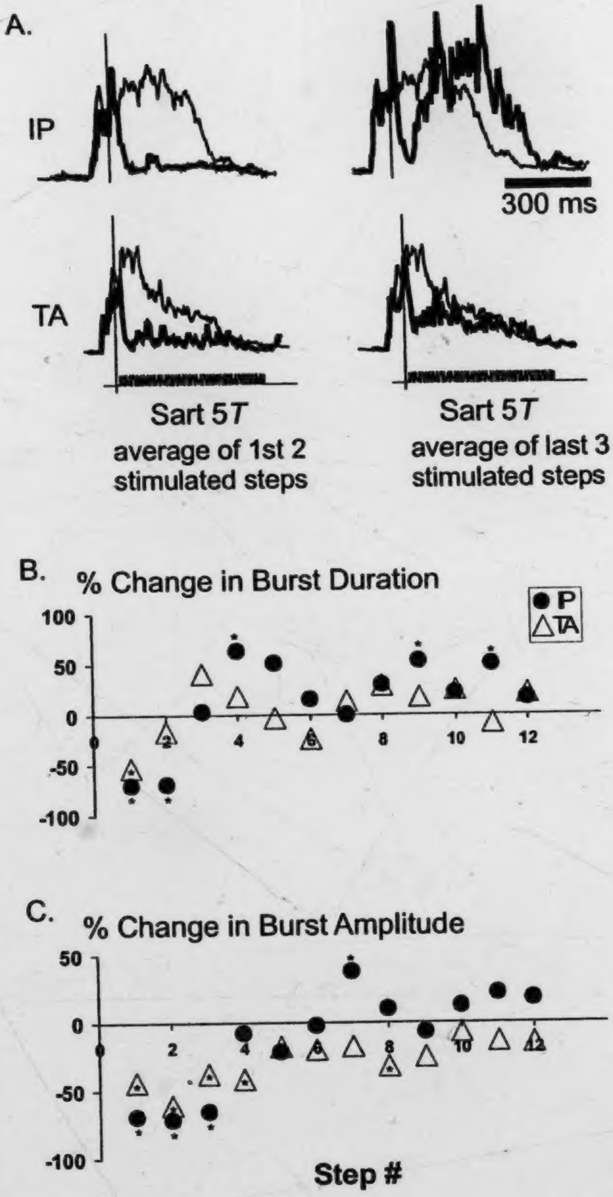
Table 4.1. Effects of 3-5 T Sartorius Nerve Stimulation.

For each cat, the number of walking sequences in which each type of effect in response to 3-5 *T* sartorius nerve stimulation was tabulated. The numbers in brackets indicate the number of steps that were stimulated.

	Cat 1	**Cat 2**	**Cat 3**
gradual change from inhibitory to excitatory effect	5 (n = 10-20)	8 (n = 8-35)	1 (n = 17)
all inhibitory effect		2 (n = 6-8)	1 (n = 4)
all excitatory effect	1 (n = 10)		
variable excitatory and inhibitory effects with no pattern	1 (n = 5)	1 (n = 22)	

Figure 4.5. The Effect of 5T Sartorius Nerve Stimulation on Flexor Burst Activity during Locomotion.

A) Thick lines represent averaged iliopsoas (IP) and tibilias anterior (TA) EMG during stimulated steps and thing lines represent averaged IP and TA EMG during control steps (n = 15). The left panel shows the strong inhibitory effect with stimulation of the sartorius nerve at 5 *T* at the beginning of a walking trial. This inhibitory effect gradually reverses to an excitatory effect on IP activity at the end of the same walking sequence (right panel) while TA activity returns closer to control levels. The gradual change in effect from inhibitory to excitatory is clearly seen by quantifying the percent change in burst duration (*B*) and amplitude (which was averaged over the plateau period of the burst profile). C. Filled circles represent change in IP burst activity and open triangles represent TA burst activity. Asterisks (*) denote steps that were significantly different from control ($p < 0.05$).

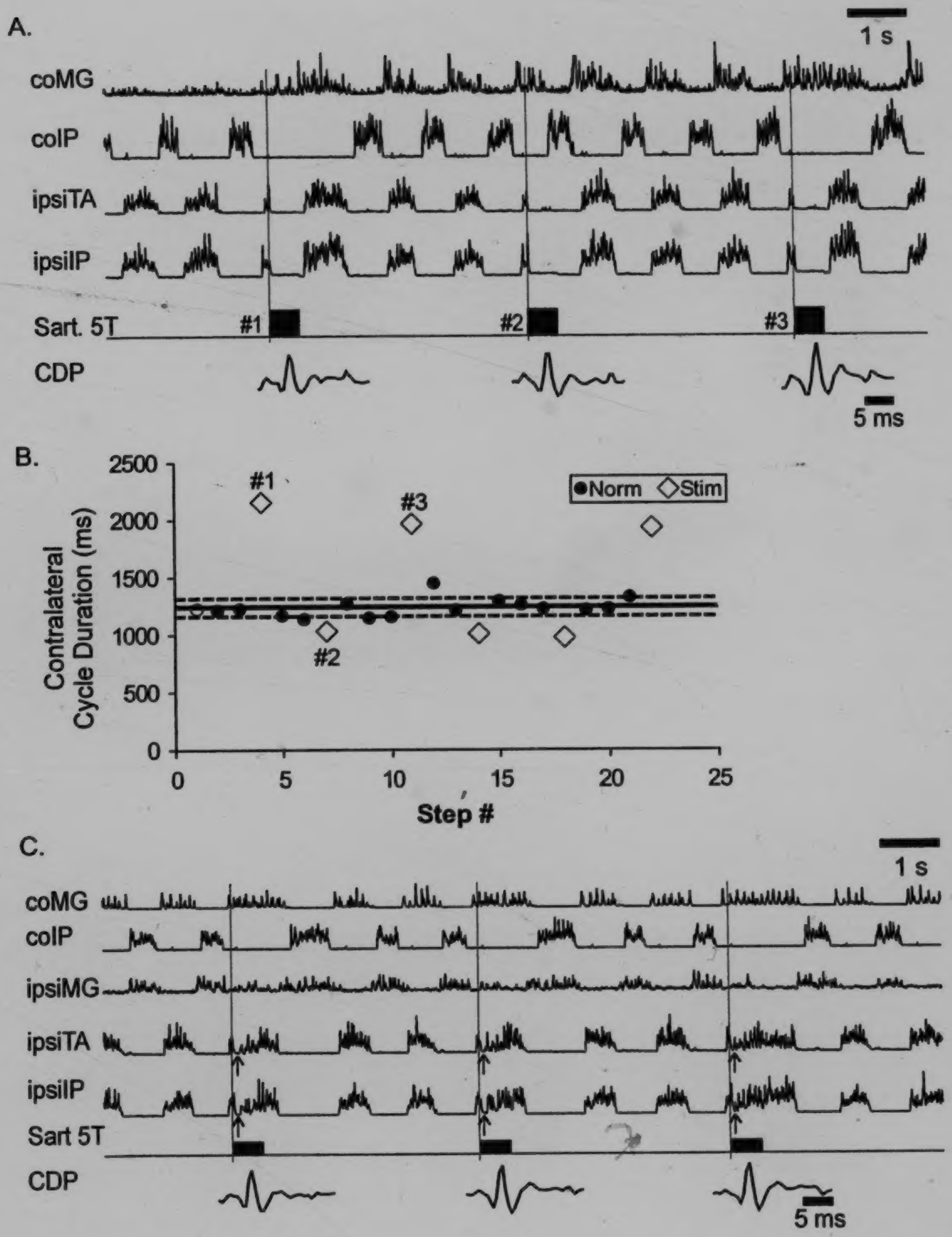

A.
IP
TA
300 ms
Sart 5*T*
average of 1st 2
stimulated steps
Sart 5*T*
average of last 3
stimulated steps
B.
% Change in Burst Duration
● P
△ TA
100
50
0
-50
-100
0
2
4
6
8
10
12
C.
% Change in Burst Amplitude
50
0
-50
-100
0
2
4
6
8
10
12
Step #

muscle, the inhibitory effect decreased almost to zero in the latter half of the stimulation. Figure 4.5B and C quantifies this change in the effect of sartorius group II stimulation over time. At the beginning of the trial, both the IP and TA burst durations and amplitudes are lower than control (Fig. 4.5B and C) ($p < 0.05$, denoted by asterisks). Burst durations of the IP and TA returned very quickly to control (within 3 stimulation trials in this example). By the end of the walking sequence, IP burst duration was consistently higher than control ($p < 0.05$, denoted by asterisks) while TA burst duration increased to a level closer to control values (Fig. 4.5B). The amplitude of the IP and TA EMGs showed a decrease in the initial stages of the walking sequence with stimulation of the sartorius nerves at group II strength ($p < 0.05$, denoted by asterisks). By the end of the walking sequence, IP burst amplitude tended to be slightly higher than control steps. The TA EMG amplitude increased, but to a lesser extent and remained slightly below control values (Fig. 4.5C). Note that the emerging excitatory effect in the IP muscle was preceded by an inhibitory effect on burst duration, which matched that seen in earlier stages of the walking sequence. Similarly, in the TA muscle, the initial inhibitory effect was followed by a secondary excitatory effect not seen in the early stages of the walking sequence. This effect was seen in many of the locomotor sequences when stimulation of the sartorius nerve at group II strengths yielded the pattern of transition from inhibitory to excitatory effects (e.g. also indicated by arrows in Fig. 4.6C).

The effect of group II sartorius nerve stimulation on the timing of the locomotor cycle usually varied in conjunction with the varying effect on flexor burst duration. As stated above, the most typical effect of sartorius nerve stimulation at group II strengths was initially a shortening, which gradually reversed to an excitatory effect on flexor burst

Figure 4.6. Stimulating the Sartorius Nerve at Group II Strengths Produced Varying Results.

A. In this example, 5 *T* sartorius nerve stimulation consistently produced inhibition of the ipsilateral flexor bursts, however, the effect on locomotor cycle period varied: either resetting to contralateral flexion occurred (#2) or prolongation of the contralateral cycle period occurred (#1 and #3). The varying effects on the locomotor rhythm are clearly demonstrated in *B* where shortening or prolonging the contralateral rhythm occurs randomly within a single walking sequence. The steps illustrated in A are marked in *B*. C. strong excitatory effect on ipsilateral flexor burst duration and locomotor cycle period is also possible with 5 *T* sartorius nerve stimulation. Arrows in C indicate the emergence of a secondary excitatory effect following 5 *T* sartorius nerve stimulation. Abbreviations: co, contralateral; ipsi, ipsilateral; CDP, cord dorsum potential.


A.
1 s
coMG
coIP
ipsiTA
ipsiIP
Sart. 5T
#1
#2
#3
CDP
5 ms
B.
Contralateral Cycle Duration (ms)
2500
2000
1500
1000
500
0
●Norm
◇Stim
#1
#3
#2
Step #
0
5
10
15
20
25
C.
1 s
coMG
coIP
ipsiMG
ipsiTA
ipsiIP
Sart 5T
CDP
5 ms

duration. Corresponding with the effect on flexor burst duration was a gradual change in the effect on cycle duration (Fig. 4.4*B*). Figure 4.6 illustrates other examples from one animal of the effect of activation of group II sartorius muscle afferents on the locomotor rhythm. This example is taken from one of the 6 walking sequences that did not exhibit the pattern of a gradual decrease in inhibitory effect due to group II sartorius muscle afferent stimulation. Figure 4.6A illustrates an example where sartorius nerve stimulation at group II strengths sometimes reset the locomotor rhythm by prolonging the contralateral cycle period. This is exhibited in the 1st and 3rd stimulated steps. Delivery of the stimulation train inhibited ongoing ipsilateral flexor activity. Once the stimulus train ended, ipsilateral flexor activity resumed. In the meantime, the contralateral IP remained silent. Sartorius nerve stimulation at group II strengths during flexion also sometimes reset the locomotor rhythm by halting ipsilateral flexion and advancing the onset of contralateral flexor burst activity. This is illustrated in the 2nd stimulated step in figure 4.6A. Figure 4.6*B* is a scatterplot illustrating the effect of sartorius nerve stimulation at 5 *T* on the contralateral cycle period in the stepping sequence that is partly illustrated in figure 4.6A. Stimulated steps are represented by the open diamonds and control steps by the filled circles. In this sequence, stimulation of the sartorius nerve at group II strengths caused resetting of the contralateral rhythm, either by shortening or lengthening the period between successive contralateral IP bursts. Figure 4.6C illustrates an example where stimulation of the sartorius nerve at 5 *T* during the swing phase produced a prolongation of ongoing IP and TA burst duration and cycle duration. The effect of group II strength stimulation of the sartorius nerve was dramatic, resulting in an almost doubling of the duration of the flexor bursts compared to control steps. Note that the main excitatory effect was preceded by a short inhibition (indicated by arrows). This example is taken from the latter stages of a walking sequence that had shown the pattern of gradual decrease in inhibition with successive stimulus trains of 5 *T* to the sartorius nerve.

4.4 Discussion

An important key to understanding how the nervous system regulates the production of locomotion is identifying the role of afferent feedback pathways in shaping locomotor output. Such feedback provides important sensory cues necessary for walking to be functional during changing conditions. Many investigations have examined the modulation of motoneuron output by cutaneous and muscle afferent feedback pathways during locomotion (reviewed in Burke 1999; McCrea 2001). In recent years, more information about the modulation of flexor activity by muscle afferent feedback pathways has accumulated, primarily from fictive preparations (Perreault et al. 1995; Degtyarenko et al. 1998; Quevedo et al. 2000). The identification of the specific muscle receptors involved and whether their feedback connections are functional during real walking remains to be determined in more detail. The work presented in this paper focused on this latter issue. The main results of this study confirm predictions from investigations on fictive preparations that feedback from sartorius group I and II muscle afferents strongly modulates ongoing flexor activity during treadmill walking in decerebrate cats. Sartorius group I muscle afferent feedback supports flexor burst generation during the swing phase of treadmill walking. Sartorius group II muscle afferent feedback was shown to have multiple effects, suggesting that multiple feedback pathways from these afferents allow flexibility in regulating swing phase activity during walking and consistent with previous apparently contradictory findings from fictive locomotor preparations (Perreault et al. 1995; McCrea et al. 2000).

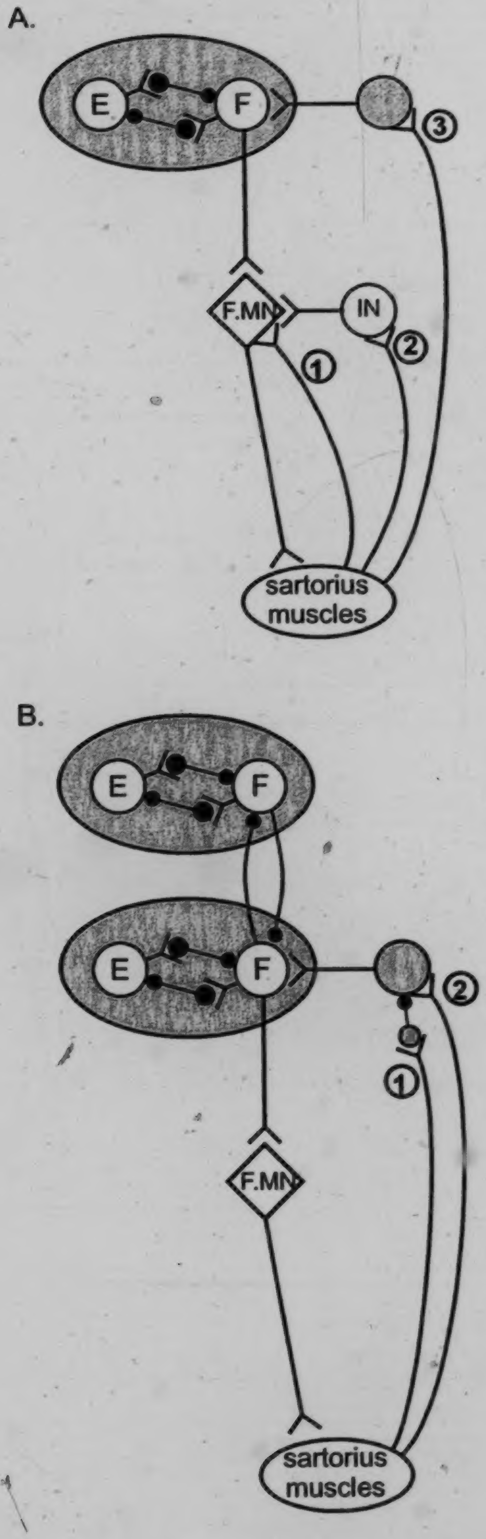
4.4.1 *Action of Sartorius Group I Muscle Afferents*

Previous results from this laboratory have shown that proprioceptive feedback is important for regulating the magnitude and duration of flexor activity during the swing phase of decerebrate cat locomotion (Lam and Pearson 2001a). Resisting flexion, thereby increasing load and length inputs to hip flexor muscles, caused an increase in hip flexor activity. Assisting flexion, thereby unloading and prematurely shortening the hip flexor muscles, caused the opposite effect. Moreover, proprioceptive feedback from the sartorius muscles was found to be particularly important for this effect since denervation of the sartorius muscle diminished the response to resisting hip flexion. Lam and Pearson (2001a) proposed that group I afferents, particularly from the sartorius muscles, were likely candidates for mediating this response in decerebrate walking cats. Results from the present study confirm and extend this proposal. Low-threshold stimulation ($\leq 1.4\ T$) of group I sartorius muscle afferents resulted in an increase in the magnitude of IP EMG without any significant effect on IP burst duration or TA burst activity. Higher-threshold activation at group I strengths ($\geq 1.6\ T$) of the sartorius nerve was effective in prolonging the duration of both IP and TA bursts as well as the amplitude of the IP EMG. In figure 4.3*B*, an example from walking sequences where the locomotor rhythm was also significantly affected by sartorius nerve stimulation at group I strengths was shown. It is important to note that in these walking sequences, the ipsilateral extensor bursts were weak. Thus, input from the extensor rhythm, which is normally strongly entrained by the speed of the treadmill, was weaker and provided appropriate conditions for revealing the strong effects on ipsilateral flexion and cycle duration by higher-threshold strength group I sartorius nerve stimulation.

There are two possible pathways by which the effect on IP amplitude could be mediated. The first is the monosynaptic pathway from Ia sartorius muscle afferents to IP motoneurons (Eccles and Lundberg 1958) (*pathway 1*, Fig. 4.7A). The second is a disynaptic excitatory pathway between sartorius group I afferents to IP motoneurons described in fictive locomotor cat preparations (Quevedo et al. 2000) (*pathway* 2, Fig. 4.7A). Such disynaptic excitation on homonymous and synergist motoneurons was elicited by mechanical stimuli that would activate only muscle spindle afferents as well as by electrical stimulation ranging in strength from 1.4 to 2 *T* (in the range that would recruit both group Ia and Ib fibers in the stimulated nerve) (Quevedo et al. 2000). The fact that there is an effect on both IP and TA burst durations as well as cycle period with higher stimulus intensities (between 1.6 and 1.8 *T*) suggests that group I muscle afferents can also act at the level of the rhythm generator to influence locomotor timing (*pathway* 3, Fig. 4.7A). Based on the present data, we suggest that maximal recruitment of large-diameter fibers is required to influence the locomotor rhythm. However, we also cannot rule out the possibility that differential recruitment of Ia and Ib fibers may have been a factor in the separate effects on IP burst amplitude and duration with different stimulus strengths (i.e. ≤ 1.4 *T* and ≥ 1.6 *T*) (Jack 1978), although this cannot be established with certainty by grading the stimulus intensity as used in the present experiments.

Figure 4.7. Schematic Diagram of Sartorius Muscle Afferent Feedback Pathways Involved in the Modulation of Flexor Activity during Locomotion.

A. Group I muscle afferent feedback pathways can act on the motoneuron monosynaptically (1), via a disynaptic excitatory pathway (2), or by access to the flexor half-centre of the locomotor pattern generator (3). *B.* Group II muscle afferent feedback pathways have multiple access to the flexor half-centre of the locomotor pattern generator by inhibitory (1) and excitatory (2) connections. Black or grey-shaded dots represent inhibitory connections. Inverted arrows represent excitatory connections. E, extensor. F, flexor. MN, motoneuron. See Discussion for more details.


A.
E
F
③
F.MN
IN
①
②
sartorius muscles
B.
E
F
E
F
②
①
F.MN
sartorius muscles

4.4.2 Action of Sartorius Group II Muscle Afferents

Results from previous studies showed that the effects of sartorius group II muscle afferent electrical stimulation on flexor burst activity during fictive locomotion are variable, producing either shortening of ongoing flexor activity and resetting the locomotor rhythm to extension (Perreault et al. 1995) or a prolongation and enhancement of flexor activity (McCrea et al. 2000). These contradictory results can be taken as evidence for the existence of parallel excitatory and inhibitory pathways from group II flexor muscle afferents to flexor motoneurons. In the present study, we showed that during treadmill locomotion in decerebrate cats, stimulation of the sartorius nerve at group II strength could have either an inhibitory or an excitatory effect on ongoing flexor burst activity, usually depending on the timing of the stimulation within a walking sequence (Fig. 4.4 and 4.5). While the responses to stimulation of sartorius group II muscle afferents were variable (i.e. either excitatory or inhibitory), this variability in the responses was seen in all animals tested (Table 4.1) and support the existence of parallel excitatory and inhibitory pathways from group II flexor muscle afferents to flexor motoneurons.

In 70% of the trials, a general pattern emerged which was characterized by a gradual transition from an inhibitory to an excitatory effect as more stimulation trains were delivered. Since the 3-5 *T* sartorius nerve stimulation would activate both group I and II muscle afferents, it is possible that the transition from an inhibitory to an excitatory response was mediated by a diminishment of group II inhibition and an emergence of group I effects on flexor burst duration. This possibility is suggested by the finding that a second excitatory effect often followed an initial inhibitory effect after stimulation of the sartorius nerve at group II strengths (Fig. 4.5 and 4.6). However, given that stimulation of the sartorius nerve at group II strengths could produce excitatory or inhibitory responses separately (Table 4.1), there is also the possibility that these afferents could also act through both inhibitory and excitatory pathways to shape IP and TA burst activity. Furthermore, both inhibitory and excitatory influences from flexor group II muscle afferents to flexor burst activity have been demonstrated separately by previous results from fictive locomotor preparations (Perreault et al. 1995; McCrea et al. 2000). Depending on factors that remain to be determined, the relative strengths of these pathways may be variable. One possible factor that may determine the relative strength of these pathways is that the inhibitory connection from the group II sartorius muscle afferents to the IP and TA motoneurons is less resilient to repeated activation, since strong inhibitory effects were usually short-lived within a walking sequence (Fig. 4.4 and 4.5).

An important issue is whether sartorius group II muscle afferents have access to the locomotor rhythm generator. Previous findings showed that there is a strong resetting effect on the locomotor rhythm with stimulation of flexor group II muscle afferents during the flexor phase of fictive locomotion (Perreault et al. 1995; McCrea et al. 2000), which is strong evidence for the idea that these afferents have access to the locomotor rhythm generator (Hultborn et al. 1998). An effect on locomotor rhythm is often difficult to discern in walking preparations due to the strong entrainment of the rhythm by the treadmill speed. Typically, we observed modest effects on the overall locomotor rhythm, even with strong effects on flexor burst duration with 3-5 T stimulation of the sartorius nerve (Fig. 4.4). Despite strong entrainment by the treadmill, occasionally a strong resetting effect could be observed, as illustrated in figure 4.6. The fact that stimulation of the sartorius nerve at 3-5

T could have an effect on flexor burst duration as well as on the locomotor cycle period indicates that feedback pathways from group II sartorius muscle afferents have access to the locomotor pattern generator in walking decerebrate cats. These feedback pathways can be either inhibitory or excitatory on the locomotor rhythm generator (Fig. 4.7*B*). Further support that sartorius group II muscle afferents access the locomotor central pattern generator is provided by the fact that activity in the ipsilateral MG bursts was also affected by the stimulation. In this case, MG burst activity was suppressed or inhibited. This could be explained by insufficient disinhibition of the ipsilateral extensor half-centre even when the ipsilateral flexor half-centre was inhibited by sartorius group II muscle afferents.

Data from the present study also provide further evidence for the strong mutual inhibitory connection between contralateral flexor half-centers (Lundberg 1981). Whether stimulation of the sartorius nerve produced an inhibitory or excitatory effect on flexor burst duration and cycle duration, flexor muscles from both hindlimbs were never active at the same time (e.g. Fig. 4.6A and C). A particularly strong example of this is shown in figure 4.6C. In this case, stimulation of the sartorius nerve at 5 *T* significantly prolonged ongoing flexor activity (by almost double) yet contralateral flexor activity did not resume until the ipsilateral flexor bursts ended. Another aspect of the group II effect on the flexor half-centre is exemplified in figure 4.6A. In this case, 5 *T* sartorius nerve stimulation resulted in a dramatic shortening of ongoing flexor activity. Yet, resetting to contralateral flexion did not necessarily occur. Presumably the level of inhibition from the sartorius group II afferents can be modulated, to determine whether resetting of the locomotor rhythm to contralateral flexion is enabled or not (indicated by the grey-shaded dot in *pathway* 2, Fig. 4.7*B*).

4.4.3 *Functional Implications and Concluding Remarks*

Results from this study further support the idea that sartorius group I muscle afferents support and, if necessary, augment ongoing flexor activity during treadmill locomotion. Such mechanisms could serve important roles in modulating the level of flexor activity in response to different locomotor tasks, such as uphill walking (Carlson-Kuhta et al. 1998) or stepping over obstacles (McFadyen et al. 1999). We have also shown data supporting the idea that the sartorius group II afferents have access to both inhibitory and excitatory pathways to the ipsilateral flexor half-centre. This would provide the flexibility that is necessary during the swing phase of locomotion when a variety of potentially unstable conditions is often unexpectedly encountered. In such situations, stereotyped reactions to a given input (e.g. muscle length from secondary muscle spindles) may not always provide functional or helpful responses during the swing phase.

4.5 References

Andersson O, Grillner S. Peripheral control of the cat's step cycle. II. Entrainment of the central pattern generators for locomotion by sinusoidal hip movements during "fictive locomotion". *Acta Physiologica Scandinavica* 118: 229-239 1983.

Burke RE. The use of state-dependent modulation of spinal reflexes as a tool to investigate the organization of spinal interneurons. *Experimental Brain Research* 128: 263-277, 1999.

Carlson-Kuhta P, Trank TV, Smith JL. Forms of forward quadrupedal locomotion. II. A comparison of posture, hindlimb kinematics, and motor patterns for upslope and level walking. *Journal of Neurophysiology* 79: 1687-1701, 1998.

Conway BA, Hultborn H, Kiehn O. Proprioceptive input resets central locomotor rhythm in the spinal cat. *Experimental Brain Research* 68: 643-656, 1987.

Degtyarenko AM, Simon ES, Norden-Krichmar T, Burke RE. Modulation of oligosynaptic cutaneous and muscle afferent reflex pathways during fictive locomotion and scratching in the cat. *Journal of Neurophysiology* 79: 447-463, 1998.

Duysens J, Pearson KG. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Research* 187: 321-332, 1980.

Eccles RM, Lundberg A. Integrative pattern of Ia synaptic actions on motoneurones of hip and knee muscles. *Journal of Physiology* 144: 271-298, 1958.

Hiebert GW, Gorassini MA, Jiang W, Prochazka A, Pearson KG. Corrective responses to loss of ground support during walking. II. Comparison of intact and chronic spinal cats. *Journal of Neurophysiology* 71: 611-622, 1994.

Hiebert GW, Pearson KG. Contribution of sensory feedback to the generation of extensor activity during walking in the decerebrate cat. *Journal of Neurophysiology* 81: 758-770, 1999.

Hiebert GW, Whelan PJ, Prochazka A, Pearson KG. Contribution of hind limb flexor muscle afferents to the timing of phase transitions in the cat step cycle. *Journal of Neurophysiology* 75: 1126-1137, 1996.

Hultborn H, Conway BA, Gossard J-P, Brownstone R, Fedirchuk B, Schomburg ED, Enríquez-Denton M, Perreault M-C. How do we approach the locomotor network in the mammalian spinal cord? *Annals of the New York Academy of Sciences* 860: 70-82, 1998.

Jack JJB. Some methods for selective activation of muscle afferent fibres. In: *Studies in Neurophysiology*, edited by R Porter. Cambridge, UK: Cambridge University Press, 1978, pp. 155-176.

Kriellaars DJ, Brownstone RM, Noga BR, Jordan LM. Mechanical entrainment of fictive locomotion in the decerebrate cat. *Journal of Neurophysiology* 71: 2074-2086, 1994.

Lam T, Pearson KG. Proprioceptive modulation of hip flexor activity during the swing phase of locomotion in decerebrate cats. *Journal of Neurophysiology* 86: 1321-1332, 2001a.

Lam T, Pearson KG. The effects of stimulating sartorius muscle afferents during the swing phase of walking in decerebrate cats. *Society for Neuroscience Abstracts* 27: 1060, 2001b.

Lundberg A. Half-centres revisited. In: *Regulatory Functions of the CNS. Motion and Organization Principles, vol.1 Advances in Physiological Sciences*, edited by J Szentagothai, M Palkovits and J Hamori. Budapest: Pergamon Press, 1981, pp. 155-167.

McCrea DA. Spinal circuitry of sensorimotor control of locomotion. *Journal of Physiology* 533: 41-50, 2001.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233,2000.

McFadyen BJ, Lavoie S, Drew T. Kinetic and energetic patterns for hindlimb obstacle avoidance during cat locomotion. *Experimental Brain Research* 125: 502-510, 1999.

Orlovskii GN, Shik ML. Standard elements of cyclic movement. *Biophysics* 10: 935-944,1965.

Pearson KG, Ramirez JM, Jiang W. Entrainment of the locomotor rhythm by group Ib afferents from ankle extensor muscles in spinal cats. *Experimental Brain Research* 90: 557-566, 1992.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Stein RB, Misiaszek JE, Pearson KG. Functional role of muscle reflexes for force generation in the decerebrate walking cat. *Journal of Physiology* 525: 781-791, 2000.

Whelan PJ, Hiebert GW, Pearson KG. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Experimental Brain Research* 103: 20-30, 1995.

CHAPTER 5

LOADING OF THE LIMB DURING THE SWING PHASE: ADAPTIVE STRATEGIES FOR STEPPING OVER OBSTACLES

5.1 Introduction

The ability to adjust the motor output of the hindlimb during the swing phase of walking is essential if an animal is to traverse over constantly changing and unpredictable terrain. During the swing phase of walking, the trajectory of the leg must be precisely regulated to avoid hitting obstacles in its path and the subsequent placement of the paw is important in order to ensure and maximize stability for the ensuing support phase. Indeed, the precise control required for the swing phase of locomotion is underlined by observations that cortical and descending input play essential roles during skilled locomotor tasks, which require such precise regulation of limb trajectory (e.g. stepping over obstacles) and placement of the foot or paw (e.g. stepping along a horizontal ladder) (Beloozerova and Sirota 1993; Widajewicz et al. 1994; Kably and Drew 1998; Prentice and Drew 2001).

How are the neural commands that are used to avoid obstacles during locomotion altered in response to changes to the biomechanical or neuromuscular properties of the limb? The sensitivity of the locomotor rhythm generator to sudden, short-lived alterations in proprioceptive or cutaneous inputs from the limb has been examined in detail by a variety of investigators (e.g. Pearson 1995; Rossignol 1996; Zehr and Stein 1999; Duysens et al. 2000). An important consequence of this sensitivity is that it can be exploited by the locomotor system to detect sustained changes in limb properties and thus gradually adjust the locomotor output to meet the new demands of the altered system. One example of this is the adaptive increase in the activity of the ankle extensor muscle medial gastrocnemius (MG) during the stance phase of walking following denervation of its synergist muscles (Whelan et al. 1995; Whelan and Pearson 1997; Misiaszek and Pearson 2002). This adaptive increase has been shown to involve an increase in the gain of feedback pathways from MG muscle afferents to the locomotor pattern generator (Whelan and Pearson 1997), to the MG motoneurons (Pearson et al. 1999; Pearson and Misiaszek 2000), and an increase in central drive from the locomotor pattern generator or descending inputs (Gritsenko et al. 2001). Descending input also plays an important role in the adaptive changes to the locomotor pattern following ankle flexor neurectomy since spinalization following adaptation to a denervation injury reveals disorganized locomotor patterns that were not present when supraspinal input was intact (Carrier et al. 1997).

Adaptive changes to the locomotor pattern can also occur in response to proprioceptive changes not associated with nerve injury. For example, decerebrate ferrets adapted to the presence of a rod in front of their forelimb by increasing their forelimb trajectory during treadmill locomotion (Lou and Bloedel 1988). Removal of the obstacle revealed a persistent increase in paw trajectory, which gradually returned to control levels. Similar after-effects are also observed in human subjects after a period of walking on a circular treadmill (Gordon et al. 1995; Weber et al. 1998) after walking on a split-belt treadmill (Prokop et al. 1995), and after running on a treadmill (Anstis 1995). The significance of the observation of an after-effect indicates that a long-term adaptive change (learning) had occurred to adjust the motor program to the constant perturbation. Removal of the disturbance reveals this adaptive learning in the form of an exaggerated movement (e.g. persistent high stepping after removal of the obstacle to forelimb swing trajectory (Lou and Bloedel 1988)). In other words, the animal had learned to perform the motor task in the presence of the disturbance by adjusting some parameter of the motor output. When the disturbance is removed, the adjustments remained and produced the after-effect. After-effects are usually short-lived, disappearing soon after the return to control conditions. In the case of the decerebrate ferrets, resumption of a normal forelimb trajectory occurred within 7 steps after removal of the rod (Lou and Bloedel 1988). Thus, the motor program can re-adapt to control conditions once the disturbance is removed.

The objective of the present study was to examine whether long-term adaptation was involved in the response to additional load of the hindlimb during obstacle avoidance in intact cats. The additional weight was applied such that the main effect of loading would occur during the swing phase and further challenge the ability to clear the obstacle. Both short-term (immediate) and long-term (more gradual) adaptive strategies were observed in the animals tested. Short-term, immediate adaptations suggest on-line, moment-to-moment responses to changes in sensory feedback. The more gradual, long-term adaptations suggest changes in the locomotor output due to the effects of training and experience with the extra weight (learning).

5.2 Methods

Data was obtained from 3 adult cats (2 female, 1 male) weighing between 3 and 4 kg. All experimental procedures were approved by the University of Alberta Health Sciences Animal Welfare Committee.

5.2.1 Preparation and Training

Cats were trained to walk along a custom-built horizontal walkway (2.48 m long, 0.23 m wide) with a wooden obstacle (6 cm high, 3.5 cm wide, 23 cm long) positioned across the centre of the walkway using food rewards as training incentives. After training (about 2 weeks for each animal), the animals underwent a sterile surgical procedure to implant intramuscular fine-wire recording electrodes (Cooner Wire AS632, Cooner Wire Company, Chatsworth CA) in the following muscles of one hindlimb: iliopsoas (IP), anterior head of sartorius (SartA), medial head of sartorius (SartM), semitendinosus (ST), and medial gastrocnemius (MG). In *cat* 2, the rectus femoris (RF) muscle was also implanted. The IP muscle has primarily a hip flexor action with some lumbar spine flexion. The SartA muscle is a hip flexor and knee extensor while the SartM is a hip and knee flexor. ST is a hip extensor and knee flexor and RF is a hip flexor and knee extensor. Unfortunately, the electrodes in the SartM muscle were damaged partway through the experimental period in *cat* 1 and *cat* 3, thus only partial data from this muscle can be presented. Electrode leads were threaded under the skin to a connector affixed externally to the top of the skull. To eliminate cutaneous input from the skin around the shank of the leg and dorsum of the paw, the sural, saphenous, and superficial peroneal nerves were transected. Following surgery, animals recovered in an incubator and were administered analgesics.

After recovery (2 to 3 days post-surgery), electromyographic (EMG) and video recording commenced. Markers were painted on the skin overlying the bony landmarks of the hip (greater trochanter), knee (knee joint line), ankle (lateral malleolus of the tibia), and metatarsal-phalangeal (head of the 5th metatarsal) joints.

Experiment 1: After collecting baseline data (1 to 2 days), a weight, weighing 100 grams, was taped to the cat's shank while the cat was anesthetized. The mass of the extra weight was equivalent to the mass of the shank segment, or 1/3 of the total mass of the hindlimb. The weight was a long strip of lead (2.5 cm wide, 16.5 cm long, and 3 mm thick) and was firmly affixed to the shaven skin over the shank by wrapping it around the shank, securing it with athletic tape, and finally binding it with VetWrap™ (3M) to prevent the animal from chewing the tape off and detaching the weight. Thus, the animal performed its usual daily activities without restrictions, with the weight on at all times during the experimental period. Daily activities included 2-4 hours of time outside the cage during which animals were seen to roam their housing area, climb, and jump. The remainder of the day was spent in their respective cages (which were about 1 m^3). Animals were brought to the lab once daily and recording of locomotor activity with the weight on continued for 7 days in *cat 1* and for 6 days in *cat 2*. After this time, the weight was removed and recording of locomotor activity continued for 4 days in *cat 1* and for 6 days in *cat 2*. During each daily recording session, the animals performed from 20 to 40 steps over the obstacle (for half of these steps, the experimental hindlimb was ipsilateral to the camera).

Experiment 2: In the second experiment, the same procedure as in *experiment 1* was followed except that the nerve to the ST muscle was exposed and cut under sterile procedure before the weight was taped to the leg. Note that the nerve branch to the ST muscle travels with the nerve to the posterior biceps (Pb) muscle, thus denervating the ST muscle in this way would also eliminate the nerve supply to the Pb muscle (a hip extensor and knee flexor muscle). Two cats underwent this procedure to cut the posterior biceps/semitendinosus (PbST) nerve. *Cat 1* had been used in *experiment 1*, but the opposite leg was used and only video data was recorded from this cat. In addition, *cat 1* often paused before stepping over the obstacle during these sets of experiments. Thus, data from this aspect of the study will be focused on those obtained from *cat 3*. In *cat 3*, the nerve to the gracilis muscle was also cut 10 days after the neurectomy of the PbST nerve and addition of the weight. The gracilis muscle is a hip extensor and adductor as well as a knee flexor. In conjunction with the hamstrings muscles and the flexor digitorum longus muscle, the gracilis muscle is active during late stance and early swing to help push the leg off the ground and generate the initial lifting of the leg for clearance (Yakovenko et al. 2002). At the time of completion of this chapter, analysis on data collected during the period between the denervation of the gracilis muscle and the removal of the weight was incomplete. Thus, the presentation of results pertaining to *experiment* 2 will just focus on the effects of PbST neurectomy on the response to additional weight and the response after removal of the weight. *Cat* 3 had the weight on for a total of 20 days (after the 10th day, the nerve to the gracilis muscle was cut). After the weight was removed from *cat* 3, recording of locomotor activity continued for 3 days. As in *experiment 1*, about 20 to 40 steps over the obstacle was performed by *cat* 3 during each daily recording session.

5.2.2 Data Analysis

Video data was recorded at 30 frames per second using a Panasonic VHS camera (shutter speed: 1/250 s). The video was inspected to identify and select those steps during which the animal did not pause during the stepping sequence before it stepped over the obstacle. The first and second hindlimbs that step over the obstacle are defined as the leading and trailing hindlimbs, respectively. The two-dimensional coordinates of the joint markers were then digitized at 30 Hz (Adobe Premiere 4.0, Adobe Systems Inc., San Jose, CA). The raw coordinate data was then digitally filtered using a dual-pass, second-order Butterworth filter at a low-pass of 10 Hz. Because of slippage of the skin over the knee joint, the x- and y-coordinates of the knee were determined trigonometrically using limb segment lengths.

To determine the extent of out-of-plane movement, the length of the segments of the leg, as seen by the video camera, was measured from each frame of video. If in any of the video frames this length varied by more than 10% from the actual length of the segment, measured directly from the animal, the data set from that step was not used in the analysis. From the 3 cats, a total of 361 steps were digitized. Of these steps, 86 were rejected based on out of plane movement. Cubic spline interpolation was applied to the raw coordinate data to increase the sampling rate to 1000 Hz. Visual inspection to compare the raw coordinate data with the filtered and splined data confirmed adequate smoothing of the data with minimal loss of the real movement trajectory. The filtered and splined coordinate data was used to calculate joint angles (hip, knee, and ankle). For the purposes of presenting kinematic results, the hip joint angle was defined as the clockwise angle from the proximal thigh segment to the horizontal plane. The knee joint angle was defined as the clockwise angle from the distal thigh segment to the proximal shank segment. The ankle joint angle was defined as the clockwise angle from the proximal foot segment to the distal shank segment (see inset stick figure in Fig. 5.1). Thus, for all joints, decreasing values correspond with greater flexion. The marker placed over the head of the 5th metatarsal was used to plot paw trajectory.

First- and second-order derivation was performed on the filtered and splined coordinate data to calculate the velocity and acceleration of the hindlimb segments. Because the acceleration profile calculated in this way was often discontinuous due to the 3rd order of the spline, the acceleration data was passed through a digital Butterworth filter (low pass between 25 and 35 Hz) to smooth the data before including it in the calculations of intersegmental dynamics. Visual inspection to compare the original acceleration data with the filtered data confirmed smoothing of the data with minimal effect on the actual acceleration profile. However, some data was inevitably lost during periods when the acceleration plot peaked and changed direction. All attempts were made to maximize smoothing while minimizing these losses during the peaks of the acceleration profile. Two-dimensional inverse dynamic analysis was then performed to calculate the torques (net, muscle, gravitational, and interaction) at the hip, knee, and ankle generated during the swing phase of stepping over the obstacle using the method described in Hoy and Zernicke (1985, 1986; also see Appendix 1).

For ease of presentation, kinematic and joint torque plots were normalized to 100% of swing phase duration. Since cats were allowed to walk at their own pace, the velocity of their stepping was not controlled. The velocity of movement during the swing phase was calculated from the displacement of the hip measured by the video recordings. The average velocity of *cat 1* was 0.80 ± 0.19 m/s. The average velocity of *cat 2* was 0.50 ± 0.12 m/s, and that of *cat 3* was 0.56 ± 0.12 m/s. The velocity of stepping with the weight on was not significantly different from that of stepping with no weight within each animal (Student's *t*-test, $p < 0.05$) (see Table 5.1).

The analog data (raw EMG signals and force transducer signal) was recorded on tape using a Vetter 4000A PCM machine. The EMG analog data filtered with a band-pass filter (high pass 10 Hz, low pass 30 Hz), full-wave rectified, and then digitized at a sampling rate of 500 Hz and stored on computer using a data acquisition system (Axotape 2.0.2, Axon Instruments). Custom written computer software programs were used to average and plot the digitized EMG traces for each stepping condition. EMG burst

Table 5.1. Comparison of Swing Phase Velocity (m/s) between Cats and between Stepping Conditions.

	No Weight	**Weight On**
Cat 1	0.82 ± 0.20	0.72 ± 0.13
Cat 2	0.51 ± 0.13	0.49 ± 0.09
Cat 3	0.58 ± 0.13	0.56 ± 0.12

amplitude was measured over a 100 ms period, usually beginning 50 ms after the onset of the burst (indicated by the thick horizontal bars positioned under the EMG records from control steps in the relevant figures). For the ST muscle, EMG burst amplitude was measured over a 100 ms period beginning at the onset of the burst. For the MG muscle, the burst amplitude was measured for 100 ms beginning at the onset of IP burst activity (see Fig. 5.10). Differences in kinematic variables and EMG were tested using student's t-test and the significance level was set at $p < 0.01$. In cases where the data set had a sample size of 1, a z-test was used to assess differences ($p < 0.01$).

Since the focus of this project was to describe the adaptive strategies to the additional weight and not to describe differences between trailing and leading limbs over the obstacle, the presentation of the results from *experiment 1* will focus mainly on trailing steps over the obstacle, for the sake of brevity. Adaptive strategies to the weight were similar between leading and trailing steps over the obstacle within each cat. In addition, when the PbST nerve was cut (*experiment 2*), more errors (hitting the obstacle) were committed during trailing steps over the obstacle. For these reasons, the results will focus mainly on data from the trailing limb. However, some differences in the kinematic and EMG patterns did emerge between trailing and leading steps over the obstacle, and these will be briefly discussed.

5.3 Results

Loading the limb during the swing phase of walking was achieved by affixing a lead weight to the shank. Cats were required to step over a 6.5 cm high obstacle (about 25% of total hindlimb length) while walking along a horizontal platform. This study examined the adaptive modifications made by the cats in response to loading of the limb while performing this skilled locomotor task.

5.3.1 Obstacle Avoidance with Loading of the Limb – Trailing over the Obstacle

Data from 2 cats are presented in the first part of this study. Although both cats showed evidence for long-term adaptation to the extra weight on their limbs, they each showed different adaptive strategies. For this reason, the data from each cat will be presented separately.

5.3.1a Cat 1 – Kinematics and EMG Patterns

Figure 5.1 summarizes the overall kinematic results recorded during trailing steps over the obstacle from *cat 1*. When the weight was added, there was an immediate increase in paw trajectory height ($p < 0.01$, Fig. 5.1*D*) and knee and ankle flexion (thick solid lines, Fig. 5.1A). These variables increased to an even greater degree by Day 1 with the weight on ($p < 0.01$, Fig. 5.1C and *D*) (dotted lines, Fig. 5.1A). By Day 5 with the weight on, movement of the limb generally returned to control values (thin solid lines, Fig. 5.1A). When the weight was removed from *cat 1*, after-effects were observed as a persistent increase in paw trajectory, which lasted through Day 1 (thick solid line and dotted line, Fig. 5.1*B*). The maximum paw trajectory height on Day 0 after weight removal was significantly greater than control ($p < 0.01$, Fig. 5.1*D*). Knee flexion angle also tended to be greater than control on Day 0 after weight removal, but this was not significant (Fig. 5.1*B*). By Day 3 after the weight was removed, paw trajectory and joint angles returned to close to control values (Fig. 5.1*B*-*D*).

Figure 5.2 shows the muscle activation patterns from trailing steps over the obstacle from *cat 1*. There was an immediate increase in ST and IP amplitude (Fig. 5.2A). The

Figure 5.1. Cat 1 – Kinematic Patterns from Trailing Steps over the Obstacle.

Paw trajectory and joint angle profiles from the hindlimb of *cat 1* during trailing steps over the obstacle with the weight on (*A*) and after the weight was removed (*B*). Smaller values correspond with greater flexion at the joints (see inset stick figure). Thin solid line with gray shading represents the averaged values from control steps and standard deviation of control steps (respectively). Each trace was normalized to 100% of the swing phase, beginning at paw lift-off. The number of steps (n) contributing to each average is indicated. C. Scatterplot graph of the slope of the paw trajectory during control steps and steps taken with the weight on and after the weight was removed. *D*. Scatterplot graph of the peak height of the paw trajectory during control steps and steps taken with the weight on and after the weight was removed. In both C and *D*, average and standard deviation values from control steps are also indicated by the solid and dotted lines, respectively. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).

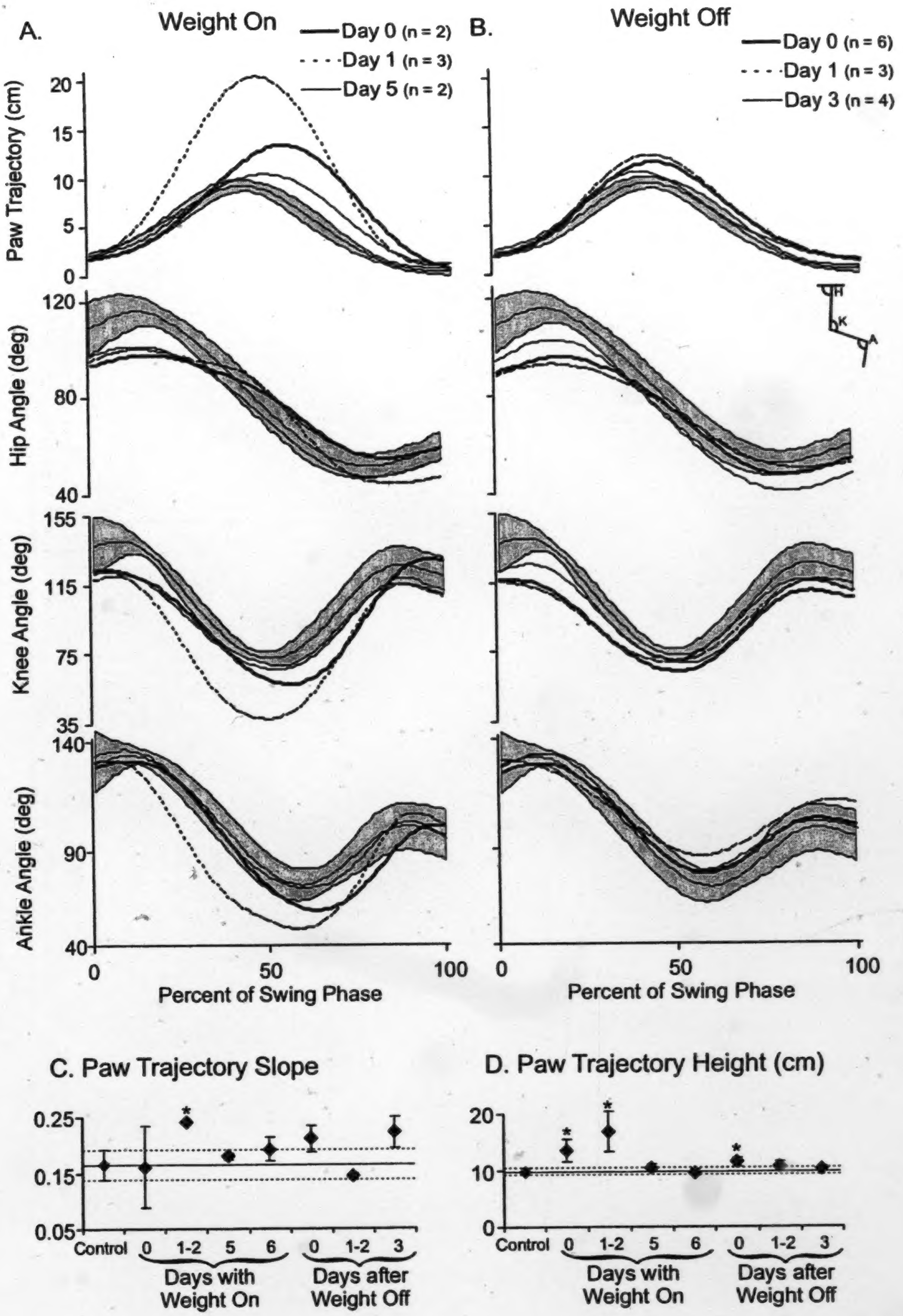
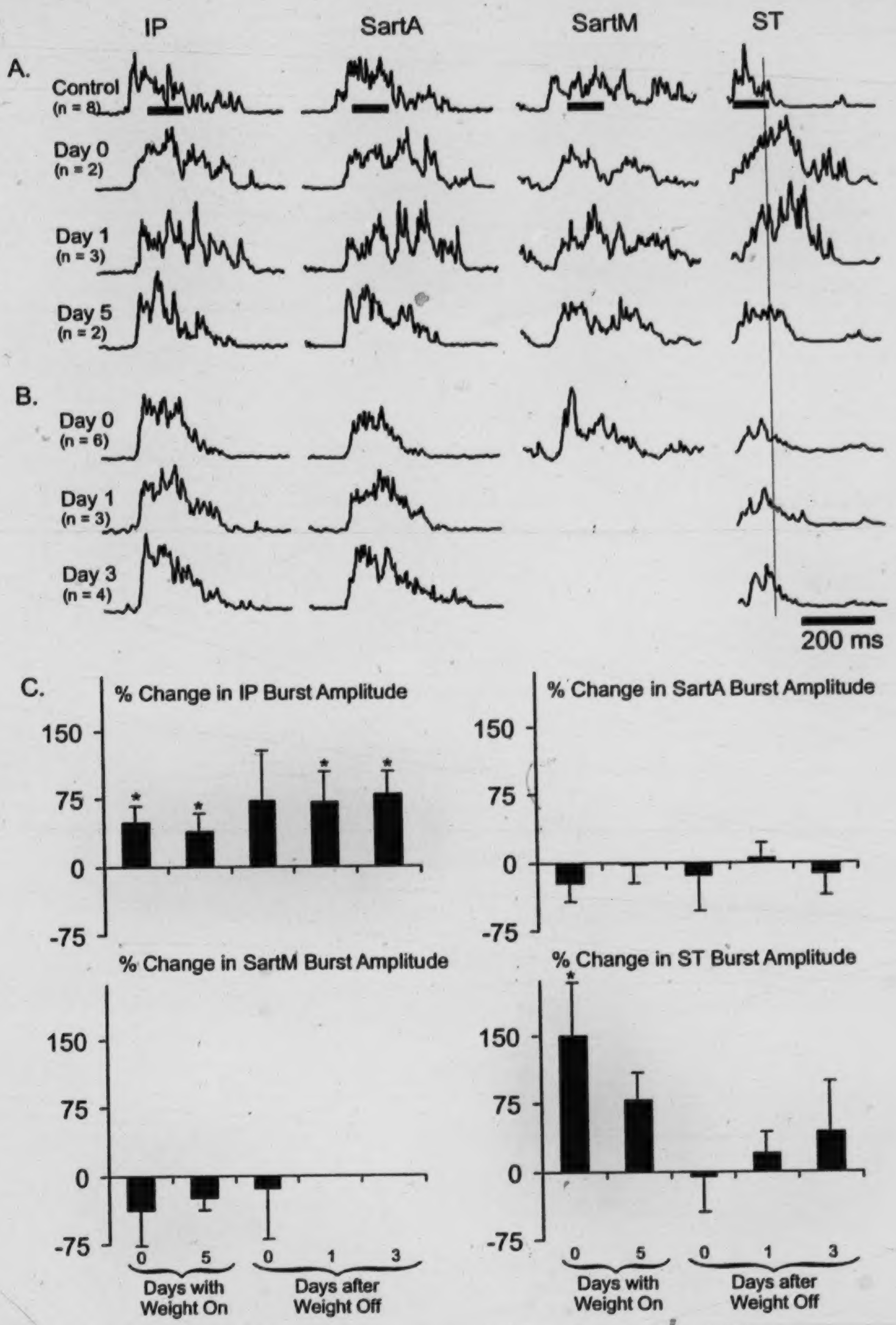

A.
Weight On
Day 0 (n = 2)
Day 1 (n = 3)
Day 5 (n = 2)
B.
Weight Off
Day 0 (n = 6)
Day 1 (n = 3)
Day 3 (n = 4)
Paw Trajectory (cm)
Hip Angle (deg)
Knee Angle (deg)
Ankle Angle (deg)
H
K
A
Percent of Swing Phase
C. Paw Trajectory Slope
D. Paw Trajectory Height (cm)
Control
Days with Weight On
Days after Weight Off
*

Figure 5.2.Cat 1 – EMG Patterns from Trailing Steps over the Obstacle.

EMG patterns from the IP, SartA, SartM, and ST muscles from *cat 1* during control steps and steps taken with the weight on (*A*) and after the weight was removed (*B*). Thick black bars underneath EMG traces from control steps indicate the period of the burst from which average EMG amplitude was measured. All EMG bursts are aligned to 100 ms before the onset of the IP burst. The number of steps (n) contributing to each average is indicated. C. Quantification of the change in IP, SartA, SartM, and ST EMG burst amplitude, expressed as a percentage of control. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).


IP
SartA
SartM
ST
A.
Control
(n = 8)
Day 0
(n = 2)
Day 1
(n = 3)
Day 5
(n = 2)
B.
Day 0
(n = 6)
Day 1
(n = 3)
Day 3
(n = 4)
200 ms
C.
% Change in IP Burst Amplitude
% Change in SartA Burst Amplitude
% Change in SartM Burst Amplitude
% Change in ST Burst Amplitude
150
75
0
-75
*
0
5
0
1
3
Days with Weight On
Days after Weight Off

increase in ST burst amplitude was significantly greater than control on Day 0 with the weight on and IP burst amplitude was significantly elevated on Days 0 and 5 with the weight on ($p < 0.01$, Fig. 5.2C). After the weight was removed, only IP burst amplitude remained elevated compared to control levels (Fig. 5.2B and C). IP burst amplitude remained elevated for up to 3 days after removal of the weight. No significant differences in SartA and SartM burst amplitude were measured.

5.3.1b Cat 2 – Kinematics and EMG Patterns

In *cat 2*, the trajectory of the paw and joint excursions were slightly lower on the same day as the weight was applied (Fig. 5.3A). Peak knee flexion on Day 0 with the weight on was actually lower than control values ($p < 0.01$) and was close to control values from Day 1 to Day 3 with the weight on (Fig. 5.3D). It was not until Day 4 with the weight on that there was an increase in paw trajectory and hip and knee flexion (Fig. 5.3A and C). When the weight was removed from *cat 2*, after-effects were observed as an increase in paw trajectory as well as a persistent increase in peak hip and knee flexion angle (thick solid lines, Fig. 5.3B). Maximum hip and knee flexion was significantly greater than control on Day 0 after the weight was removed ($p < 0.01$, Fig. 5.3C). A gradual return to control levels was not observed after the weight was removed, even after 6 days after the weight was removed. Peak hip and knee flexion angles tended to remain elevated above control values, although this difference was not statistically significant (Fig. 5.3C).

When the weight was added to *cat 2*, there was initially little change in the magnitude of ST activity while IP, SartA, and SartM activity appeared greater than control (Fig. 5.4A). Only the increase in SartM amplitude was significant when the weight was added ($p < 0.01$, Fig. 5.4C). By Day 4, ST burst amplitude was also significantly greater

Figure 5.3. Cat 2 – Kinematic Patterns from Trailing Steps over the Obstacle.

Paw trajectory and joint angle profiles from the hindlimb of *cat 2* during trailing steps over the obstacle with the weight on (*A*) and after the weight was removed (*B*). Smaller values correspond with greater flexion at the joints (see inset stick figure). Thin solid line with gray shading represents the averaged values from control steps and standard deviation of control steps (respectively). Each trace was normalized to 100% of the swing phase, beginning at paw lift-off. The number of steps (n) contributing to each average is indicated. C. Scatterplot graph of the peak hip flexion angle during control steps and steps taken with the weight on and after the weight was removed. *D.* Scatterplot graph of the peak knee flexion angle during control steps and steps taken with the weight on and after the weight was removed. In both C and *D*, average and standard deviation values from control steps are also indicated by the solid and dotted lines, respectively. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).

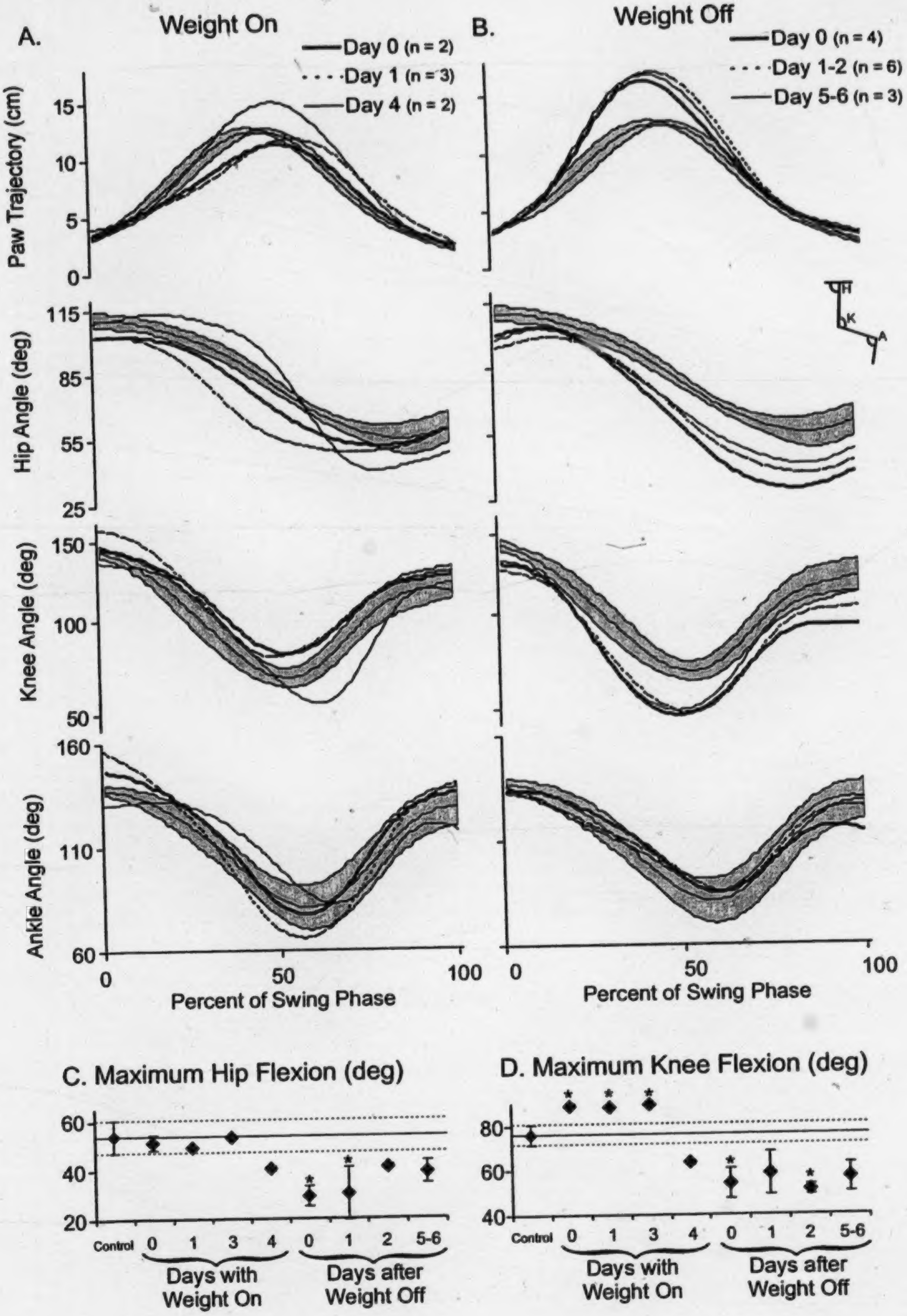
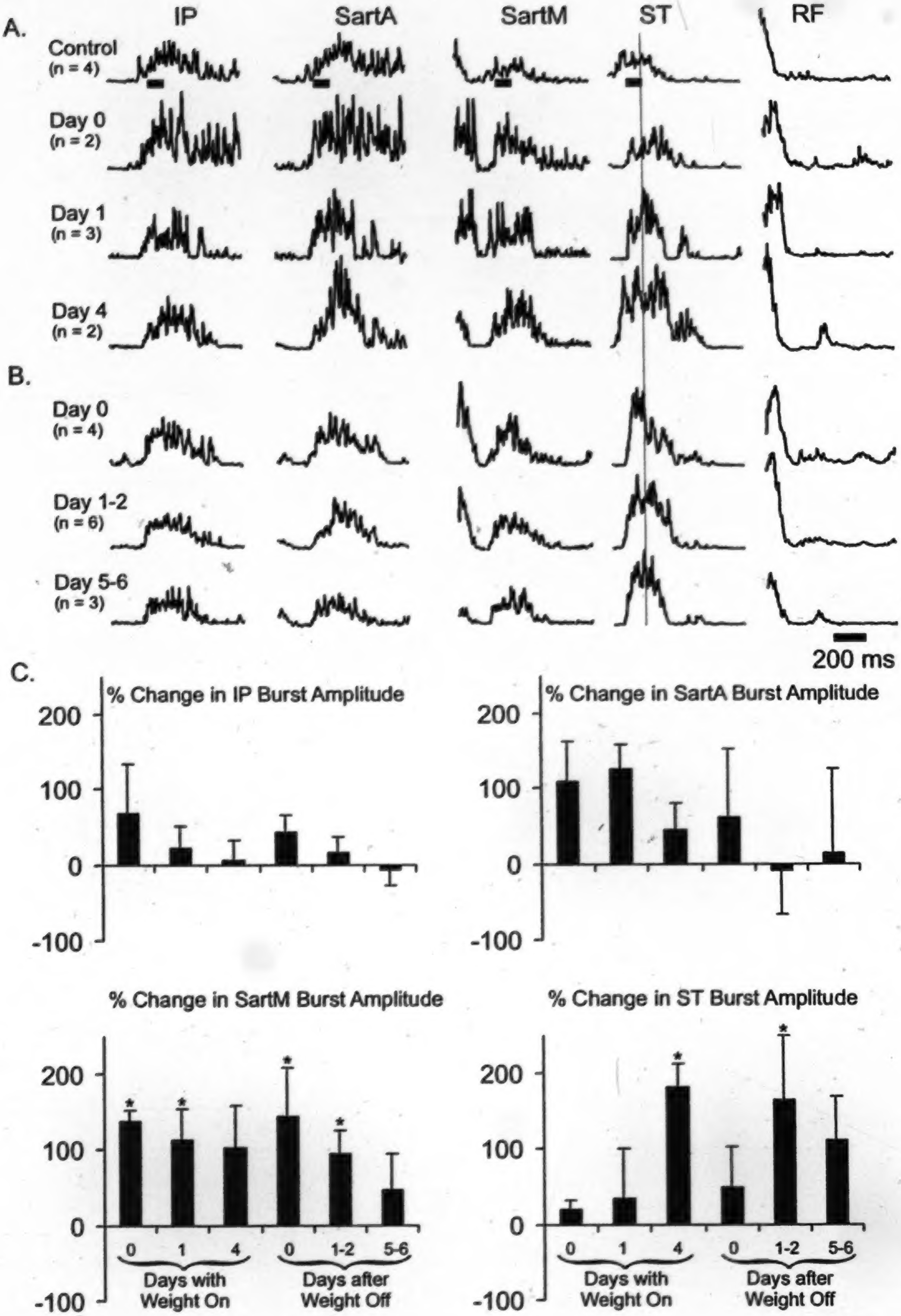

A.
Weight On
Day 0 (n = 2)
Day 1 (n = 3)
Day 4 (n = 2)
B.
Weight Off
Day 0 (n = 4)
Day 1-2 (n = 6)
Day 5-6 (n = 3)
Paw Trajectory (cm)
0
5
10
15
Hip Angle (deg)
25
55
85
115
H
K
A
Knee Angle (deg)
50
100
150
Ankle Angle (deg)
60
110
160
0
50
100
Percent of Swing Phase
C. Maximum Hip Flexion (deg)
20
40
60
Control
0
1
3
4
0
1
2
5-6
Days with Weight On
Days after Weight Off
D. Maximum Knee Flexion (deg)
40
60
80
Control
0
1
3
4
0
1
2
5-6
Days with Weight On
Days after Weight Off

Figure 5.4. Cat 2 – EMG Patterns from Trailing Steps over the Obstacle.

EMG patterns from the IP, SartA, SartM, ST, and RF muscles from *cat 2* during control steps and steps taken with the weight on (*A*) and after the weight was removed (*B*). Thick black bars underneath EMG traces from control steps indicate the period of the burst from which average EMG amplitude was measured. All EMG bursts are aligned to 100 ms before the onset of the IP burst. The number of steps (n) contributing to each average is indicated. C. Quantification of the change in IP, SartA, SartM, and ST EMG burst amplitude, expressed as a percentage of control. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).


A.
IP
SartA
SartM
ST
RF
Control
(n = 4)
Day 0
(n = 2)
Day 1
(n = 3)
Day 4
(n = 2)
B.
Day 0
(n = 4)
Day 1-2
(n = 6)
Day 5-6
(n = 3)
200 ms
C.
% Change in IP Burst Amplitude
% Change in SartA Burst Amplitude
% Change in SartM Burst Amplitude
% Change in ST Burst Amplitude
200
100
0
-100
*
0
1
4
0
1-2
5-6
Days with
Weight On
Days after
Weight Off

than control values ($p < 0.01$, Fig. 5.4C). The increase in ST burst amplitude coincides with the appearance of higher stepping in this cat at this time (see Fig. 5.3A). Generally, there was little change in the RF activity, although there was some greater flexor phase activity on Day 4 with the weight on (Fig.5.4A), which again coincides with the appearance of higher stepping. When the weight was removed, there was a persistent augmentation in flexor muscle activity, particularly in the ST and SartM muscles, both of which have flexor action at the knee (Fig. 5.4C). For up to 6 days after removal of the weight, the activity in the ST and SartM muscles tended to remain elevated, corresponding with the persistent elevation in limb flexion (see Fig. 5.3*B*).

5.3.2 Leading Steps vs. Trailing Steps over the Obstacle – Kinematics and EMG *Patterns*

The adaptive strategies to the additional weight during leading steps over the obstacle were similar to those during trailing steps for each cat. *Cat 1* showed the immediate increase in knee flexion associated with a significant increase in ST EMG activity during leading steps over the obstacle (data not shown). *Cat 2* initially showed a decrease in hip and knee flexion but after the first full day with the weight on, peak hip and knee flexion was significantly greater than control. Associated with this was a significant increase in ST EMG amplitude (data not shown). Both animals also showed after-effects (persistent high stepping) after removal of the weight during leading steps over the obstacle. The after-effects during leading steps over the obstacle lasted for the same number of days as observed during trailing steps over the obstacle for each cat.

In *experiment 2*, differences in the recovery to error-free clearance over the obstacle after adding the weight and PbST nerve cut were seen between leading and trailing steps (see next section, 5.3.3). For this reason, general differences between the kinematic and EMG patterns during leading and trailing steps over the obstacle will be summarized in this section from animals without PbST nerve cut (Fig. 5.5). Data from *cat 1* will be presented as an example, using control stepping data from figures 5.1 and 5.2 (trailing steps) to compare with control steps of leading steps over the obstacle. *Cat 2* showed similar kinematic and EMG patterns of activity during leading steps over the obstacle (data not shown).

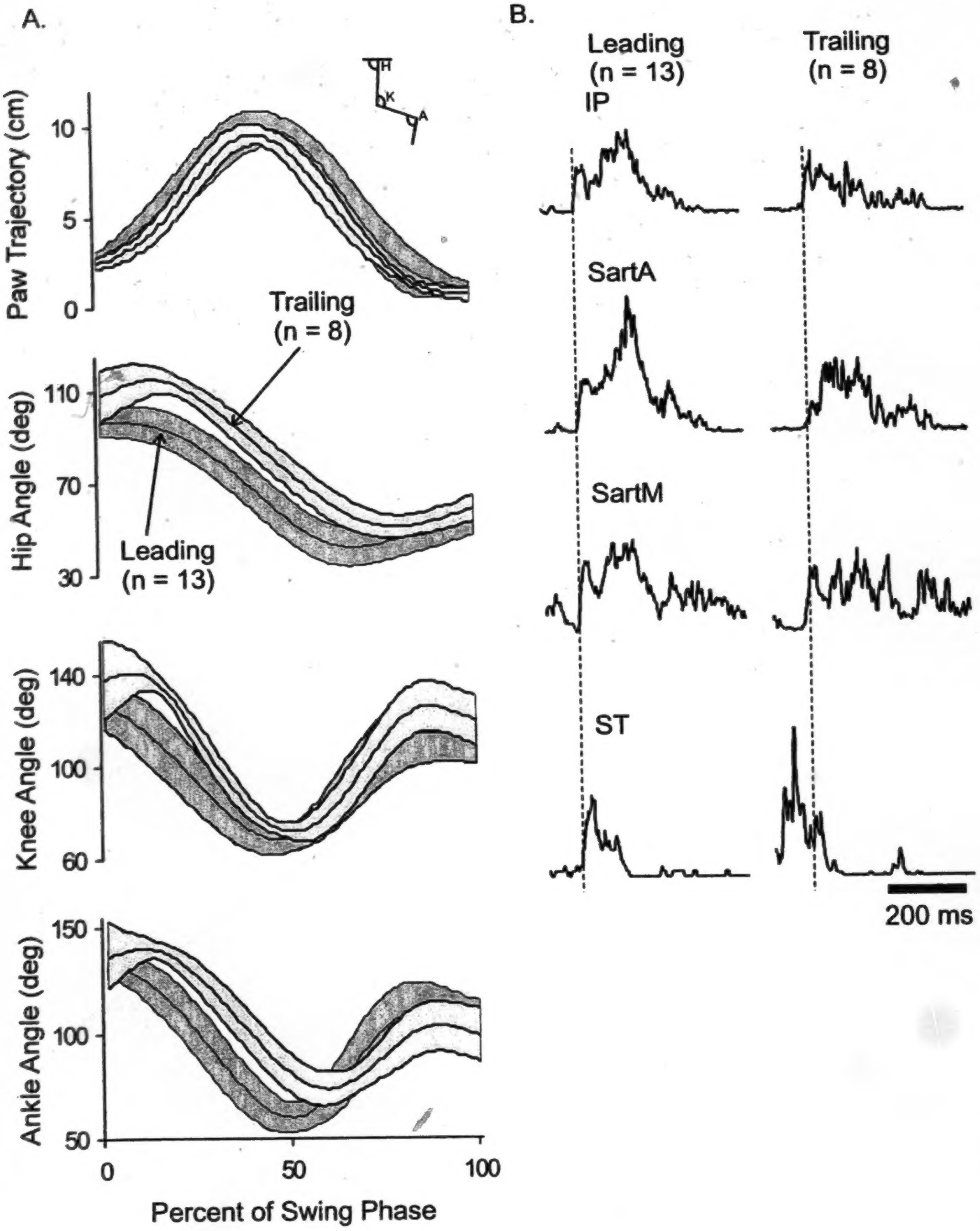
The most striking difference between leading and trailing steps over the obstacle is the greater extension at the hip at the beginning of the swing phase (Fig. 5.5A). At the beginning of swing, the average hip angle during leading steps over the obstacle was 97 degrees while that during trailing steps was 110 degrees. This difference was statistically significant ($p < 0.01$). Associated with this was an earlier onset of activity in the ST muscle (a hip extensor and knee flexor) during trailing steps over the obstacle (Fig. 5.5*B*). In addition, peak hip and ankle flexion were significantly greater during leading steps over the obstacle compared with trailing steps ($p < 0.01$, Fig. 5.5A). Activity in the hip flexor muscles (IP, SartA, and SartM) also tended to be higher during leading steps, although this was not significantly greater than that during trailing steps (Fig. 5.5*B*).

5.3.3 Obstacle Avoidance with Loading of the Limb and PbST Denervation

A striking observation during the first part of this study was the obvious recruitment of greater knee flexion that coincided with high stepping over the obstacle when the weight was added. This was apparent in both animals studied and for both leading (data not shown) and trailing steps over the obstacle. Associated with this was an increase in ST

Figure 5.5. Comparison of Kinematic and EMG Patterns during Leading and Trailing Steps over the Obstacle

A. Paw trajectory and joint angle profiles from the hindlimb of *cat 1* during leading (thin line surrounded by dark gray shaded area) and trailing steps (thin line surrounded by light gray shaded area) over the obstacle during the control condition. Smaller values correspond with greater flexion at the joints (see inset stick figure). Shaded area represents the standard deviation. Each trace was normalized to 100% of the swing phase, beginning at paw lift-off. The number of steps (n) contributing to each average is indicated. *B.* EMG patterns from the IP, SartA, SartM, and ST muscles from *cat 1* during control steps. All EMG bursts are aligned to 100 ms before the onset of the IP burst. The onset of the IP burst is indicated by the thin dashed line drawn through all the EMG traces. Note the earlier onset of ST activity compared with the onset of IP activity during trailing steps over the obstacle.


A.
H
K
A
Paw Trajectory (cm)
10
5
0
Trailing
(n = 8)
Hip Angle (deg)
110
70
30
Leading
(n = 13)
Knee Angle (deg)
140
100
60
Ankle Angle (deg)
150
100
50
0
50
100
Percent of Swing Phase
B.
Leading
(n = 13)
Trailing
(n = 8)
IP
SartA
SartM
ST
200 ms

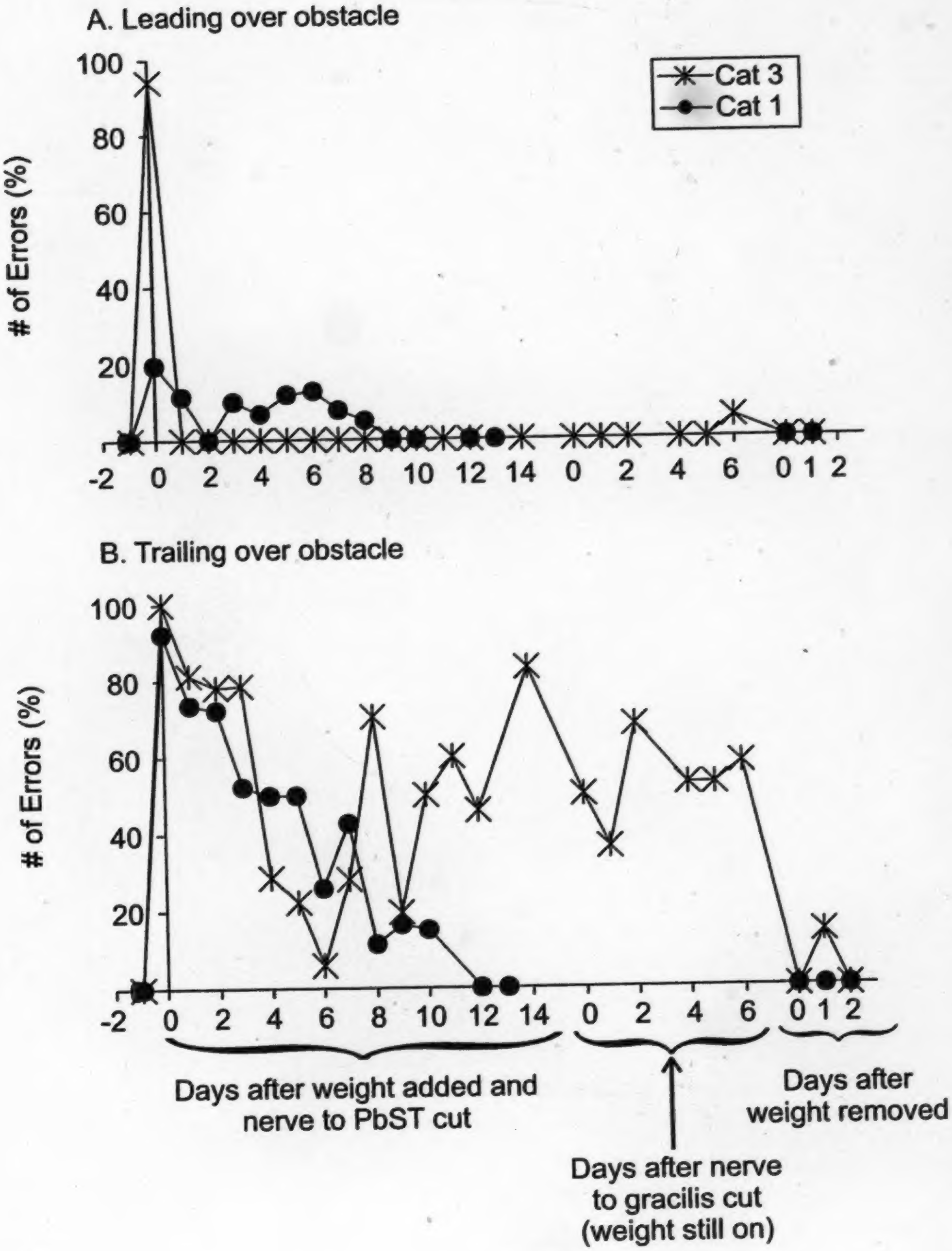
activity. Strategies that involved increases in hip or ankle flexion were also observed, but not as consistently between the animals or stepping conditions. Based on this singular role of the knee in participating in the adaptive strategies to the added weight, we wished to determine how adaptation to the weight was affected if knee flexor activity was impaired. To address this question, the nerve to PbST was exposed and cut immediately before affixing the weight to the shank (see Methods), thus preventing any force generation or sensory feedback from the Pb and ST muscles.

5.3.3a Incidence of Errors

When the PbST was denervated and the weight was added to the leg, cats were unable to step over the obstacle without contacting it. In contrast, contact with the obstacle never occurred with the weight on when the PbST was left intact. Figure 5.6 illustrates the number of errors (failure to clear the obstacle) committed by 2 animals with PbST neurectomy while they stepped over the obstacle with the weight on. When the leg was leading over the obstacle, the number of errors was relatively high in *cat 3*(about 90% of all stepping trials) on the same day that the weight was added (asterisks symbols, Fig. 5.6A). By the next day, *cat* 3 had no errors when the leg was leading over the obstacle. *Cat 1* maintained a low incidence of errors throughout the testing period, until about Day 9 (filled circle symbols, Fig. 5.6A). In *cat* 3, the nerve to the gracilis muscle was cut 14 days after the initial denervation of the PbST muscle. When this was done, there was no effect on the number of errors committed while stepping over the obstacle, except on Day 6 when the limb contacted the obstacle once out of 18 steps taken on this day (6% error rate) (filled circle symbols, Fig. 5.6A).

Figure 5.6. Number of Errors after Addition of the Weight and PbST Neurectomy during Obstacle Avoidance.

A. Incidence of errors (hitting the obstacle) during leading steps over the obstacle in cats with PbST neurectomy. The period after which neurectomy of the gracilis nerve is also indicated. Each cat is plotted separately. The incidence of errors progressively decreased over the first week with the weight on. There was no contact with the obstacle after the weight was removed. *B.* Incidence of errors during trailing steps over the obstacle in cats with PbST neurectomy, and in *cat 3*, gracilis neurectomy. Recovery of successful clearance over the obstacle when the limb was trailing was more gradual than during leading steps over the obstacle and was incomplete in *cat 3*. There was no contact with the obstacle after the weight was removed, except on Day 1 in *cat 3*.


A. Leading over obstacle
Cat 3
Cat 1
# of Errors (%)
100
80
60
40
20
-2
0
2
4
6
8
10
12
14
0
2
4
6
0
1
2
B. Trailing over obstacle
# of Errors (%)
100
80
60
40
20
-2
0
2
4
6
8
10
12
14
0
2
4
6
0
1
2
Days after weight added and nerve to PbST cut
Days after nerve to gracilis cut (weight still on)
Days after weight removed

When the leg was trailing over the obstacle, the cats had more difficulty in clearing the obstacle. *Cat 1* continued to make errors until Day 12 with the weight on after PbST nerve cut (filled circle symbols, Fig. 5.6*B*). *Cat 3*, on the other hand, showed a progressive improvement in performance until Day 6. Thereafter, performance fluctuated and never completely recovered (asterisks symbols, Fig. 5.6*B*). After the nerve to the gracilis muscle was cut in *cat 3*, there was an initial decrement in performance compared with the previous day. By the 3rd day after gracilis muscle denervation, performance levels returned to previous values (asterisks symbols, Fig. 5.6*B*).

When the weight was removed, the paw never contacted the obstacle in *cat 1* for either stepping condition (Fig. 5.6A and *B*, filled circle symbols). In *cat 3*, the paw could clear the obstacle for the majority of the steps taken after the weight was removed, with the exception of Day 1 with the weight off when errors were committed in 3 out of 21 trailing steps (14% of the steps). Recall that *cat 3* had neurectomy of the gracilis nerve by this time (see Methods). This neurectomy combined with the PbST nerve cut could have contributed to the appearance of errors even after the weight was removed.

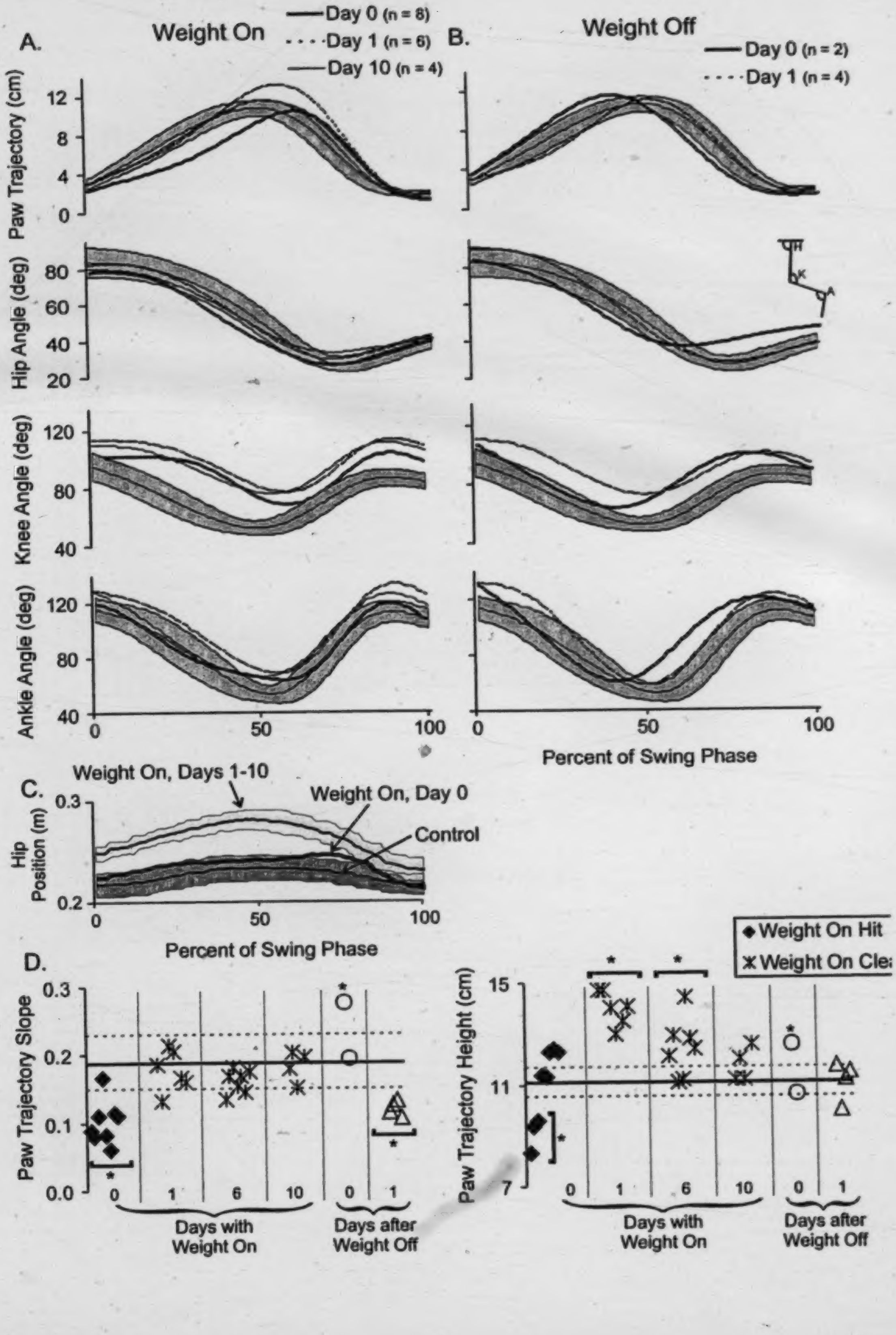
The following sections will focus on data collected from *cat 3* since a more complete data set was collected from this animal. Furthermore, as stated in the Methods section, *cat 1* often paused before stepping over the obstacle and this behaviour may have contributed to the observation that there was a low level of errors when the leg was leading over the obstacle (filled circles, Fig. 5.6A).

5.3.3b Leading Steps over the Obstacle – Kinematics, EMG Patterns, and Joint Torques

The overall kinematic patterns from leading steps over the obstacle from *cat 3* are illustrated in figure 5.7. On the same day that the weight was added, dragging of the paw

Figure 5.7. Kinematic Patterns from Leading Steps over the Obstacle after PbST Neurectomy.

Paw trajectory and joint angle profiles from the hindlimb of *cat 3* during leading steps over the obstacle with the weight on (*A*) and after the weight was removed (*B*). Smaller values correspond with greater flexion at the joints (see inset stick figure). Thin solid line with gray shading represents the averaged values from control steps and standard deviation of control steps (respectively). Each trace was normalized to 100% of the swing phase, beginning at paw lift-off. The number of steps (n) contributing to each average is indicated. C. The position of the hip marker during control steps (thin solid line surrounded by dark gray shaded area), steps taken on Day 0 with the weight on (thick solid line), and steps taken on Days 1-10 with the weight on (thin solid line surrounded by light gray area) was plotted over the normalized duration of the swing phase. Shaded areas represent standard deviation. Hip position was significantly higher during steps taken on Days 1-10 with the weight on (paired *t*-test, $p < 0.01$). *D*. Scatterplot graphs of the slope of the paw trajectory (left panel) and of the maximum paw trajectory height (right panel) during control steps and steps taken with the weight on and after the weight was removed. Average and standard deviation values from control steps are also indicated by the solid and dotted lines, respectively. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$). Filled diamond symbols represent steps taken with the weight on that hit the obstacle during the swing phase. Asterisks symbols represent steps taken with the weight on that cleared the obstacle during the swing phase. Open symbols (circles, triangles, and squares) represent steps taken after the weight was removed.


A.
Weight On
Day 0 (n = 8)
Day 1 (n = 6)
Day 10 (n = 4)
B.
Weight Off
Day 0 (n = 2)
Day 1 (n = 4)
Paw Trajectory (cm)
Hip Angle (deg)
Knee Angle (deg)
Ankle Angle (deg)
H
K
A
Percent of Swing Phase
C.
Weight On, Days 1-10
Weight On, Day 0
Control
Hip Position (m)
Percent of Swing Phase
D.
Paw Trajectory Slope
Paw Trajectory Height (cm)
Weight On Hit
Weight On Cle
Days with Weight On
Days after Weight Off

was evident (thick solid line, Fig. 5.7A) and the slope of the paw trajectory on this day was significantly lower compared to control ($p < 0.01$, Fig. 5.7*D*, left panel). During the first 3 steps after the weight was added, the maximum paw trajectory height was also significantly less than control ($p < 0.01$, Fig. 5.7*D*, right panel). Errors (hitting the obstacle) were committed in all steps taken on this day. The deficit in paw trajectory appeared to be primarily due to a deficit in knee flexion particularly over the initial half of the swing phase (Fig. 5.7A). By Day 1 with the weight on, paw trajectory slope returned to control values while the height of the paw trajectory was significantly higher than control levels ($p < 0.01$, Fig. 5.7*D*). Paw trajectory height was generally elevated throughout the period with the weight on. These observations corresponded with the fact that the cat was able to clear the obstacle during leading steps after Day 1 with the weight on. Curiously, any increase in hip, knee, or ankle joint flexion was not observed in association with greater paw trajectory height (Fig. 5.7A). However, the position of the hip was elevated compared to control on Day 1 to Day 10 with the weight on (light-gray shaded area, Fig. 5.7C). Elevation of the hip was not seen on Day 0 with the weight on (when the paw always contacted the obstacle) (thick black line, Fig. 5.7C). Thus, elevation of the hip could have been a strategy that was used to elevate the paw over the obstacle.

When the weight was removed, after-effects were seen as an increase in paw trajectory slope and height. The steeper paw trajectory corresponds with the steeper hip excursion during the initial half of swing in these steps (Fig. 5.7*B*). This after-effect was short-lived, however, as it lasted for only a few steps after removal of the weight (Fig. 5.7C). Due to out-of-plane movement, only 2 steps after removal of the weight (the 4th and 8th steps) were included in the analysis. The 4th step (first data point in the scatterplot) is representative of the first 3 steps insofar as high stepping was observed. Both paw trajectory slope and peak height were significantly higher compared to control in the 4th step after the weight was removed. By the 8th step after the weight was removed, these variables returned to control values. On the 1st day after the weight was removed, the slope of the paw trajectory was significantly lower than control values (*p* <0.01, Fig. 5.7C, left panel) while peak paw trajectory height was control values (Fig. 5.7C, right panel). Recall that by the time the weight was removed, the nerve to the gracilis muscle had also been transected (see Methods).

On the same day that the weight was added, there was an increase in IP, SartA, and SartM burst amplitude. The increase in SartA and SartM burst amplitudes were significantly greater than control on this day (*p* < 0.01, Fig. 5.8C). For the remainder of the period with the weight on, however, the amplitude of the IP and SartA muscles was not different from control and in fact tended to be lower than control. The higher IP and SartA amplitude on Day 0 with the weight on might have been related to the fact that the paw always contacted the obstacle on this day and thus represents a phasic reflex response (represented by gray-shaded bars in Fig. 5.8C). On the other hand, the increase in SartM burst amplitude persisted throughout the testing period with the weight on. Unfortunately, the recording electrodes for the SartM muscle were damaged after the weight was removed, so whether there was a persistent increase in SartM burst activity after removal of the weight could not be evaluated.

Calculations of muscle torques in this cat were valuable since good EMG recordings, lasting through the duration of the experimental period, were obtained from only a few muscles. In the plots in figure 5.9A, averages of muscle torques from steps taken on Day 1

Figure 5.8. Muscle Activation Patterns from Leading Steps over the Obstacle after PbST Neurectomy.

EMG patterns from the IP, SartA, SartM, and MG muscles from *cat* 3 during control steps and steps taken with the weight on (*A*) and after the weight was removed (*B*). Thick black bars underneath EMG traces from control steps indicate the period of the burst from which average EMG amplitude was measured. All EMG bursts are aligned to 100 ms before the onset of the IP burst. The number of steps (n) contributing to each average is indicated. C. Quantification of the change in IP, SartA, and SartM EMG burst amplitude, expressed as a percentage of control. Gray shaded bars in the bar graphs indicate that all the steps represented in the average were those that hit the block during the swing phase. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).

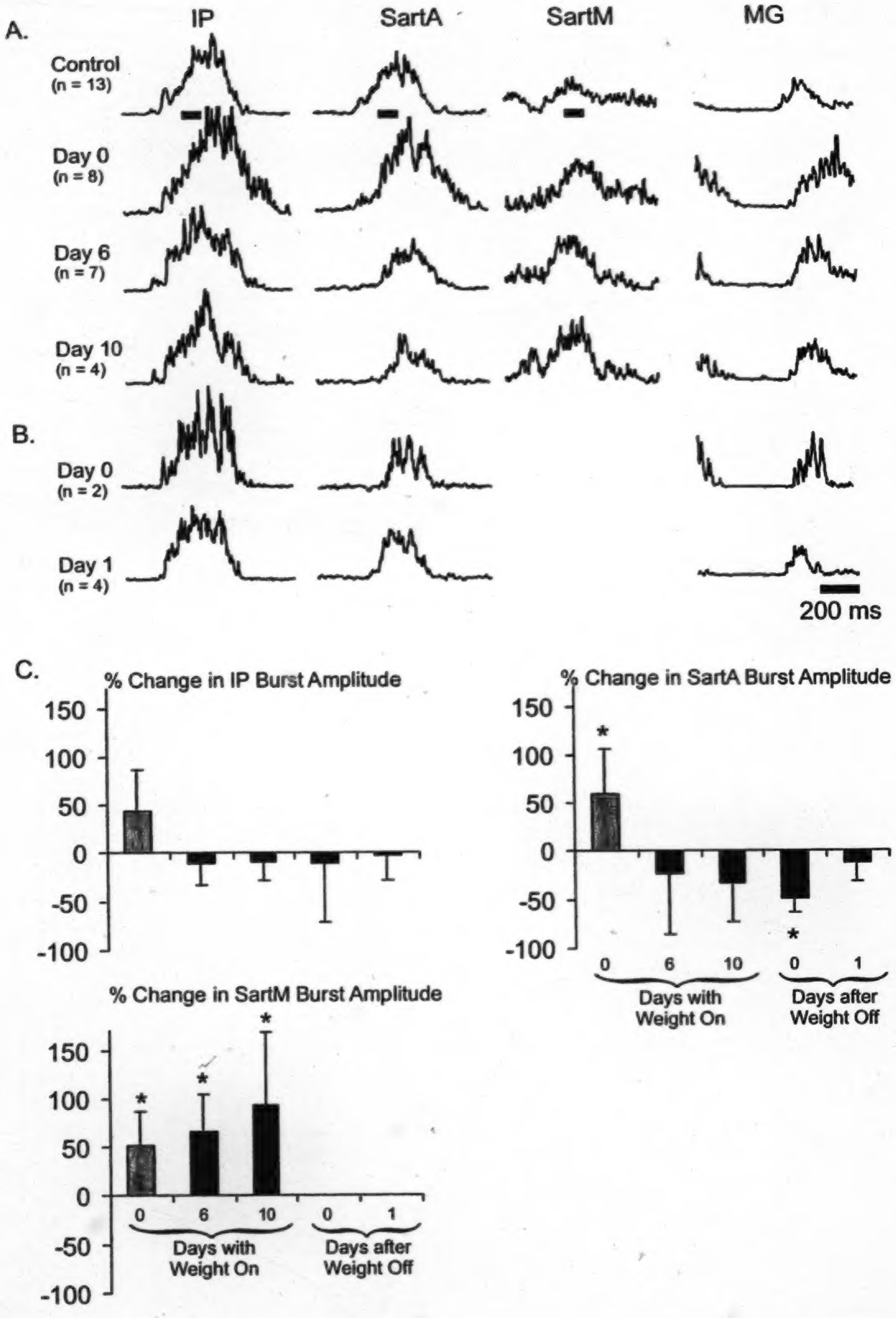
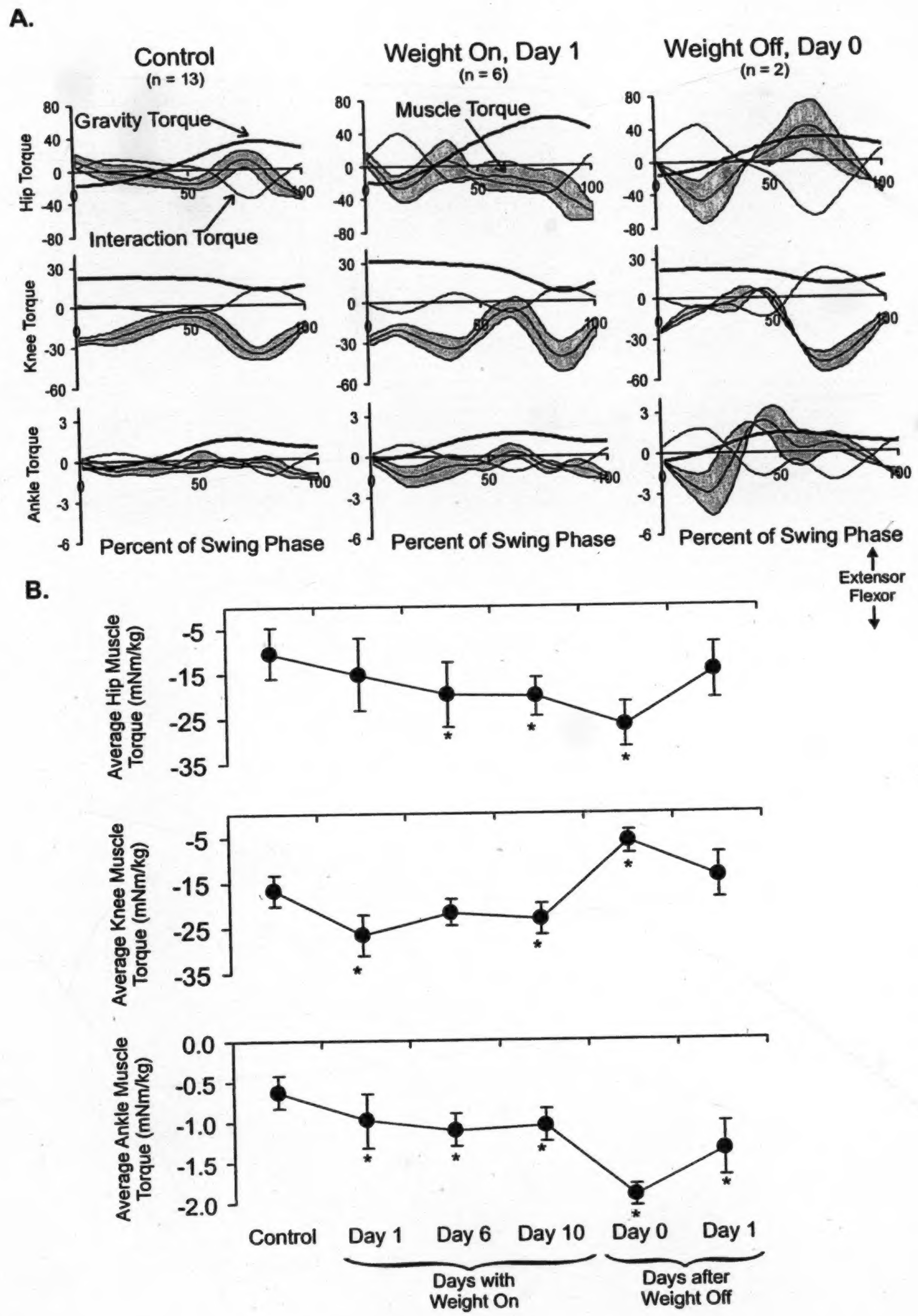

A.
IP
SartA
SartM
MG
Control
(n = 13)
Day 0
(n = 8)
Day 6
(n = 7)
Day 10
(n = 4)
B.
Day 0
(n = 2)
Day 1
(n = 4)
200 ms
C.
% Change in IP Burst Amplitude
150
100
50
0
-50
-100
% Change in SartA Burst Amplitude
150
100
50
0
-50
-100
*
*
0
6
10
0
1
Days with Weight On
Days after Weight Off
% Change in SartM Burst Amplitude
*
*
*
150
100
50
0
-50
-100
0
6
10
0
1
Days with Weight On
Days after Weight Off

Figure 5.9. Joint Torques during Leading Steps over the Obstacle after PbST Neurectomy.

Torques generated at the hip, knee, and ankle during control, weight on (Day 1), and weight off steps in *cat* 3. A. Thick solid line represents averaged gravity torque, thin solid line represents averaged interaction torques, and thin solid line with gray shaded area represents averaged muscle torque and standard deviation, respectively. Positive values indicate extensor torques and negative values indicate flexor torques. All traces are aligned to the onset of swing and normalized to 100% of swing phase duration. The number of steps (n) contributing to each average is indicated. Muscle torques in each condition were averaged over the first half of the swing phase and plotted in the scatterplots illustrated in B. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).


A.
Control
(n = 13)
Weight On, Day 1
(n = 6)
Weight Off, Day 0
(n = 2)
Gravity Torque
Muscle Torque
Interaction Torque
Hip Torque
Knee Torque
Ankle Torque
80
40
0
-40
-80
30
0
-30
-60
3
0
-3
-6
0
50
100
Percent of Swing Phase
Extensor
Flexor
B.
Average Hip Muscle Torque (mNm/kg)
-5
-15
-25
-35
Average Knee Muscle Torque (mNm/kg)
Average Ankle Muscle Torque (mNm/kg)
0.0
-0.5
-1.0
-1.5
-2.0
*
Control
Day 1
Day 6
Day 10
Day 0
Day 1
Days with Weight On
Days after Weight Off

with the weight on are presented. This was the first day in which all the leading steps successfully cleared the obstacle (see Fig. 5.6A). In these steps, there was greater generation of hip flexor muscle torque during the first part of the swing phase (Fig. 5.9A). This was short-lived, however, as hip muscle torque quickly reversed to an extensor torque. Thereafter, hip muscle torque became increasingly more flexor through to the end of the swing phase, rather than reverse to the usual decelerating hip extensor muscle torque that typically occurs at this time (compare with control stepping) (Fig. 5.9A). A possible explanation for this is that the generation of hip flexor muscle torque was a compensatory action to counteract a greater force of gravity due to the extra weight on the leg. Analysis of gravity torques at this time showed a higher level of torque due to gravity at the end of the swing phase that would have tended to pull the hip back into extension (Fig. 5.4A, middle panel). Thus, it is possible that this greater generation of hip flexor muscle torque was recruited to counteract the greater force of gravity tending to extend the hip at the end of swing. At the knee, there was more flexor muscle torque generated during swing when the weight was on despite denervation of the Pb and ST muscles (Fig. 5.9A, middle panel). Recruitment of SartM activity likely contributed to compensate for the loss of input from the Pb and ST muscles in producing knee flexion as well as assisting with hip flexion (Fig. 5.8). At the ankle, there was generally more flexor muscle torque throughout swing (Fig. 5.9A, middle panel).

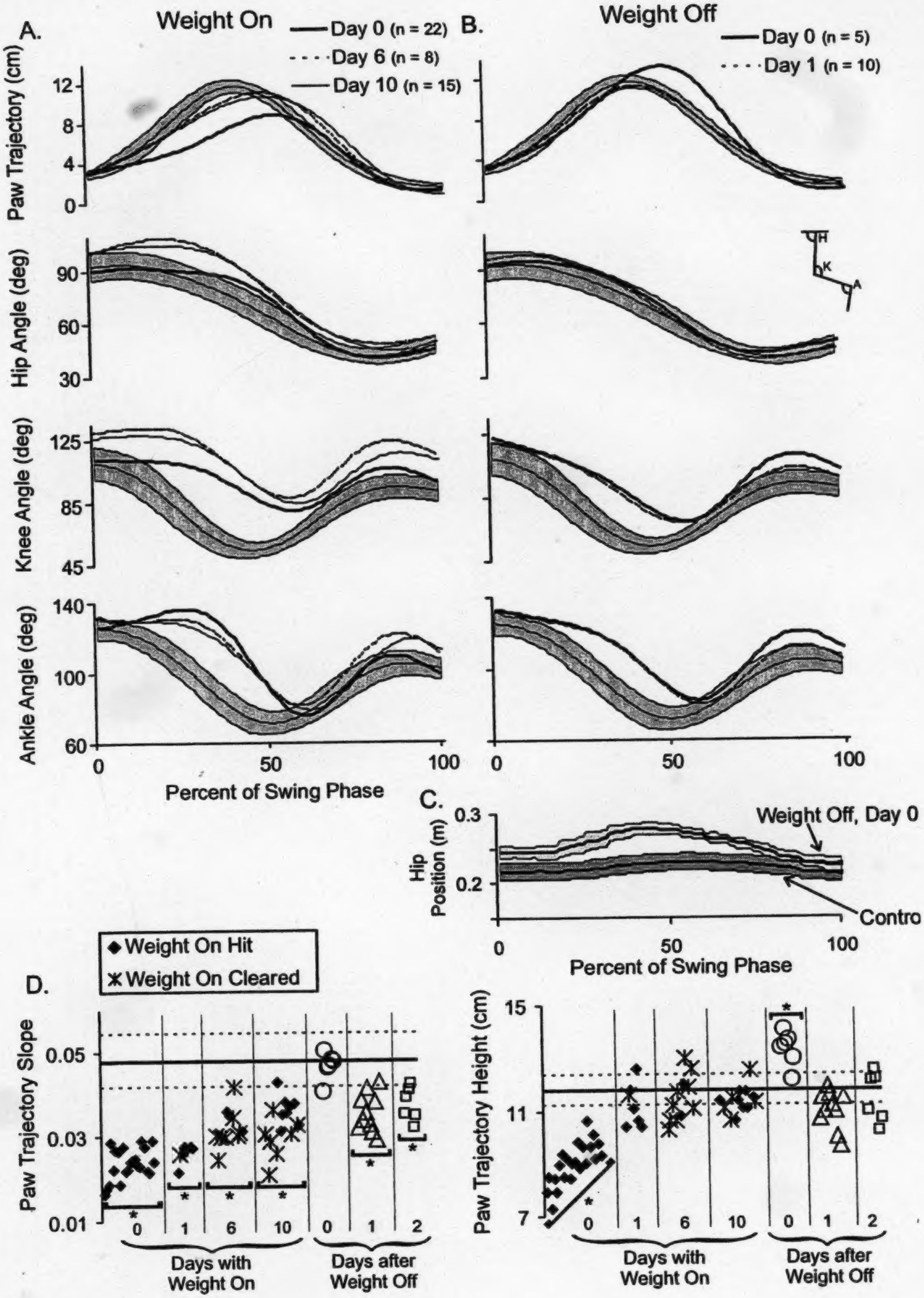
The muscle torque was averaged over the first 50% of the swing phase and plotted in figure 5.9*B*. Negative values correspond with flexor muscle torques. When the weight was on, muscle torques generated at the hip, knee, and ankle were generally greater than control values ($p < 0.01$, Fig. 5.9*B*). When the weight was removed, after-effects were discerned only by a short-lived persistent increase in paw trajectory slope and height (see Fig. 5.7*B* and C). A persistent increase in hip and ankle flexor muscle torque was measured on the same day the weight was removed ($p < 0.01$). This does not correspond with any change in EMG patterns. However, due to the limited number of EMG recordings available, changes in muscle activity were likely missed. Knee flexor muscle torque was significantly lower than control values ($p < 0.01$), which was not surprising given the denervations of the PbST and gracilis muscles and coinciding with the lower knee angle excursion compared with control values (Fig. 5.7A).

5.3.3c Trailing Steps over the Obstacle – Kinematics, EMG Patterns, and Joint Torques

More errors were observed during trailing steps over the obstacle after the weight was added in *cat* 3. On the same day that the weight was added, there was a significant decrease in the trajectory of the paw ($p < 0.01$, Fig. 5.10A and *D*). This was associated with a deficit in hip, knee, and ankle flexion (Fig. 5.10A). Although the slope of the paw trajectory gradually increased towards control levels over the 10 days with the weight on, it never achieved the same values as during control steps. In fact, paw trajectory slope was persistently lower than control values for the duration of this period ($p < 0.01$, Fig. 5.10*D*, left panel). This could account for the fact that recovery of error-free stepping over the obstacle was incomplete in this condition. On the other hand, peak paw trajectory height did return to control values by Day 1 with the weight on and remained at this level throughout the period with the weight on (Fig. 5.10*D*, right panel). However, neither the slope nor the peak height of the paw trajectory could account for the presence or absence of errors since, for example, a relatively steeper paw trajectory was occasionally measured, yet the paw still hit the obstacle (compare filled diamond with asterisks symbols, Fig. 5.10*D*, left

Figure 5.10. Kinematic Patterns from Trailing Steps over the Obstacle after PbST Neurectomy.

Paw trajectory and joint angle profiles from the hindlimb of *cat* 3 during trailing steps over the obstacle with the weight on (A) and after the weight was removed (B). Smaller values correspond with greater flexion at the joints (see inset stick figure). Thin solid line with gray shading represents the averaged values from control steps and standard deviation of control steps (respectively). Each trace was normalized to 100% of the swing phase, beginning at paw lift-off. The number of steps (n) contributing to each average is indicated. C. The position of the hip marker during control steps (thin solid line surrounded by dark gray shaded area) and during steps taken on the same day the weight was removed (thin solid line surrounded by light gray shaded area) was plotted over the normalized duration of the swing phase. Shaded areas represent standard deviation. Hip position was significantly higher during steps taken after the weight was removed (paired *t*-test, $p < 0.01$). *D.* Scatterplot graphs of the slope of the paw trajectory (left panel) and of the maximum paw trajectory height (right panel) during control steps and steps taken with the weight on and after the weight was removed. Average and standard deviation values from control steps are also indicated by the solid and dotted lines, respectively. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$). Filled diamond symbols represent steps taken with the weight on that hit the obstacle during the swing phase. Asterisks symbols represent steps taken with the weight on that cleared the obstacle during the swing phase. Open symbols (circles, triangles, and squares) represent steps taken after the weight was removed.


A.
Weight On
Day 0 (n = 22)
Day 6 (n = 8)
Day 10 (n = 15)
B.
Weight Off
Day 0 (n = 5)
Day 1 (n = 10)
Paw Trajectory (cm)
0
4
8
12
Hip Angle (deg)
30
60
90
H
K
A
Knee Angle (deg)
45
85
125
Ankle Angle (deg)
60
100
140
0
50
100
Percent of Swing Phase
C.
Hip Position (m)
0.2
0.3
Weight Off, Day 0
Contro
0
50
100
Percent of Swing Phase
D.
Weight On Hit
Weight On Cleared
Paw Trajectory Slope
0.01
0.03
0.05
*
0
1
6
10
0
1
2
Days with Weight On
Days after Weight Off
Paw Trajectory Height (cm)
7
11
15
*
0
1
6
10
0
1
2
Days with Weight On
Days after Weight Off

panel). However, the marker used to calculate paw trajectory was actually placed over the head of the 5th metatarsal and thus would not have detected flexion or extension at the toes. Such movement at the toes could have caused contact with the obstacle during the swing phase.

In the scatterplots in Fig. 5.10*D*, the steps represented by the data points grouped under *Day 0 after Weight Off* represent steps 2 to 17 immediately after removal of the weight. After-effects were seen as an elevation in the height of the paw trajectory ($p < 0.01$) and by the increase (to control values) in paw trajectory slope during the same day that the weight was removed (Fig. 5.10*D*, open circles). However, this did not correspond with any elevation in joint angle flexion. In fact, flexion at the knee and ankle remained lower than control levels (Fig. 5.10*B*). A possible reason for this is that the position of the limb was elevated without any change in the relative joint angles and thus account for only the elevation of paw trajectory height. Indeed, this was the case, as seen in figure 5.10C. On the same day that the weight was removed, the position of the hip was significantly higher than during control steps (paired *t*-test, $p < 0.01$) and thus could account for the higher paw trajectory without any corresponding change in relative joint angles. On Days 1 and 2 after the weight was removed, the slope of the paw trajectory returned to levels that were significantly lower than control ($p < 0.01$, Fig. 5.10*D*, left panel) while the peak height of the paw trajectory remained at control levels (Fig. 5.10*D*, right panel). During this period after the weight was removed, recall that the paw was seen to contact the obstacle three times (Fig. 5.6). These errors could be attributed to the fact that both the PbST and gracilis nerves were transected by this time.

Figure 5.11. Muscle Activation Patterns from Trailing Steps over the Obstacle after PbST Neurectomy.

EMG patterns from the IP, SartA, SartM, and MG muscles from *cat 3* during control steps and steps taken with the weight on (*A*) and after the weight was removed (*B*). Thick black bars underneath EMG traces from control steps indicate the period of the burst from which average EMG amplitude was measured. All EMG bursts are aligned to 100 ms before the onset of the IP burst. The number of steps (n) contributing to each average is indicated. C. Quantification of the change in IP, SartA, SartM, and MG burst amplitude, expressed as a percentage of control. Gray shaded bars in the bar graphs indicate that all the steps represented in the average were those that hit the block during the swing phase. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).

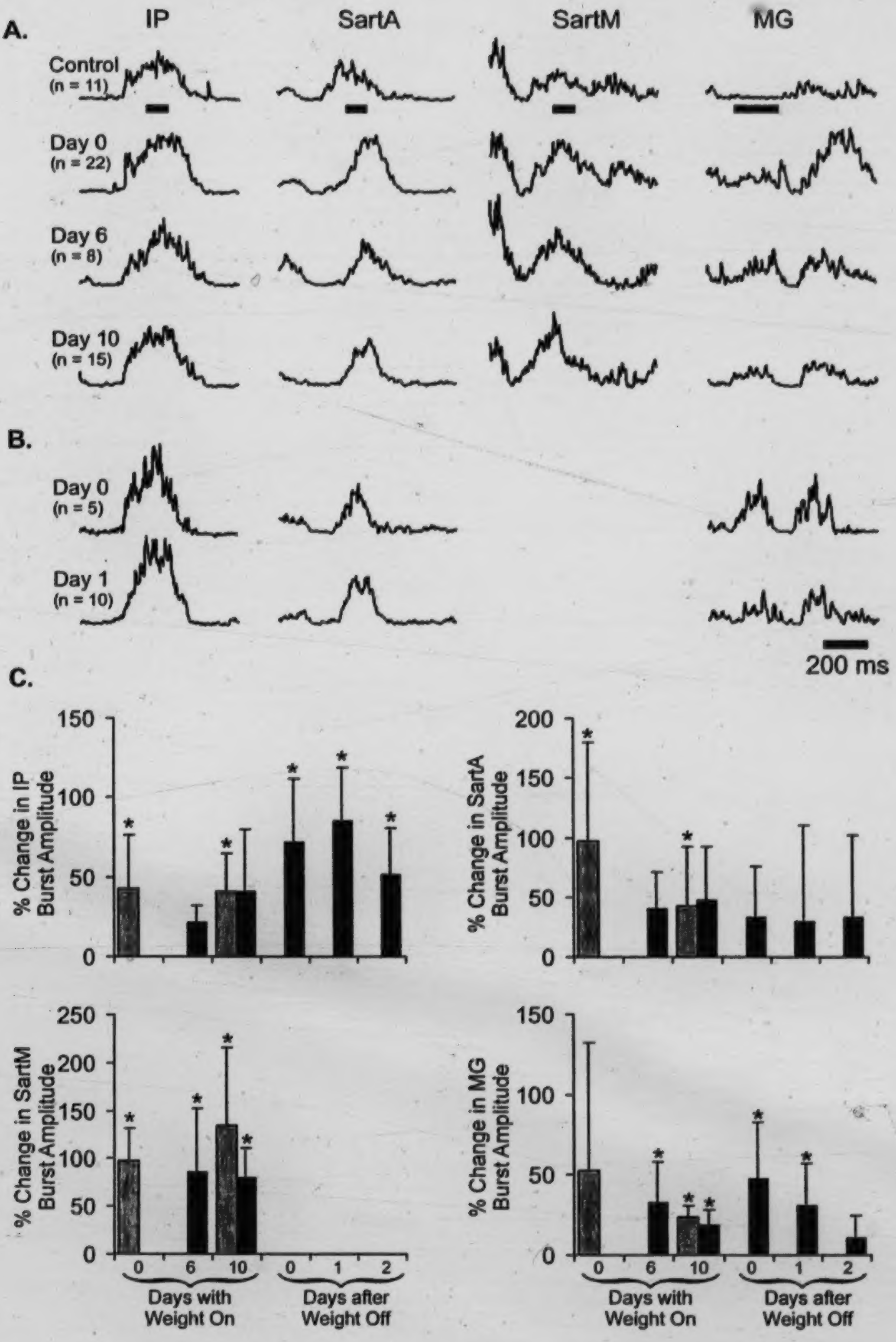
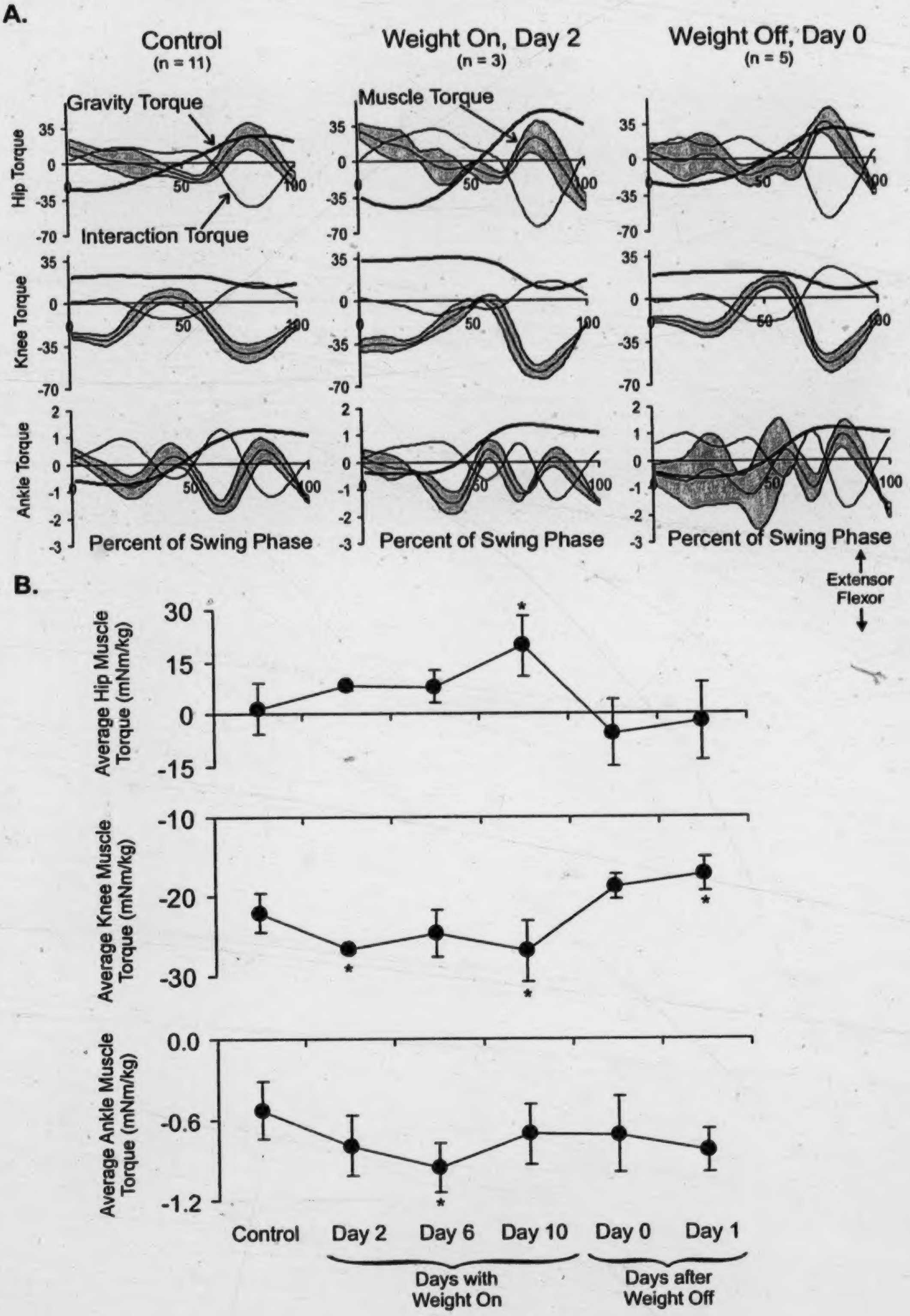

A.
IP
SartA
SartM
MG
Control
(n = 11)
Day 0
(n = 22)
Day 6
(n = 8)
Day 10
(n = 15)
B.
Day 0
(n = 5)
Day 1
(n = 10)
200 ms
C.
% Change in IP Burst Amplitude
% Change in SartA Burst Amplitude
% Change in SartM Burst Amplitude
% Change in MG Burst Amplitude
0
50
100
150
200
250
0
6
10
0
1
2
Days with Weight On
Days after Weight Off
*

Figure 5.11 illustrates EMG patterns when the weight was on and off during trailing steps over the obstacle. On Day 0 with the weight on, there was a significant increase in IP, SartA, and SartM burst amplitude ($p < 0.01$, Fig. 5.11A and C). Activity in the IP and SartM muscles, in particular, tended to be significantly elevated throughout the period with the weight on (Fig. 5.11C). A curious observation was the burst of activity in the MG muscle over the initial part of the swing phase (Fig. 5.11A). During the 10 days with the weight on, this pattern of activity in the MG muscle persisted and was usually significantly different from control ($p < 0.01$, Fig. 5.11C). This pattern was not previously observed in any other cat or in other walking conditions. It did correlate with the persistent ankle extension over the first half of the swing phase (Fig. 5.10A), which could have aided clearance over the obstacle during trailing steps. The MG muscle has its origin on the femoral condyles and thus also has knee flexor action and could have aided with clearance over the obstacle in this way. Analysis of the torques generated at the knee and ankle will help to clarify the role of this additional flexor phase activity in the MG muscle (see following paragraph). When the weight was removed, the elevation in IP burst amplitude as well as activation of the MG muscle during the flexor phase of walking persisted ($p < 0.01$, Fig. 5.11C).

In the plots of muscle torque in figure 5.12A, only those trailing steps that successfully cleared the obstacle on Day 2 with the weight on are presented. At the hip, muscle torque was more extensor and knee and ankle muscle torque was more flexor over the first part of the swing phase when the weight was on. In figure 5.12*B*, the average muscle torque over the first half of the swing phase was calculated from trailing steps that cleared the obstacle. The increase in knee flexor muscle torque over the initial half of the

Figure 5.12. Joint Torques during Trailing Steps over the Obstacle after PbST Neurectomy.

Torques generated at the hip, knee, and ankle during control, weight on (Day 1), and weight off steps in *cat* 3. A. Thick solid line represents averaged gravity torque, thin solid line represents averaged interaction torques, and thin solid line with gray shaded area represents averaged muscle torque and standard deviation, respectively. Positive values indicate extensor torques and negative values indicate flexor torques. All traces are aligned to the onset of swing and normalized to 100% of swing phase duration. The number of steps (n) contributing to each average is indicated. Muscle torques in each condition were averaged over the first half of the swing phase and plotted in the scatterplots illustrated in *B*. Error bars represent standard deviation. Asterisks (*) represents significant differences compared to control values ($p < 0.01$).


A.
Control
(n = 11)
Weight On, Day 2
(n = 3)
Weight Off, Day 0
(n = 5)
Gravity Torque
Muscle Torque
Interaction Torque
Hip Torque
Knee Torque
Ankle Torque
35
0
-35
-70
50
100
2
1
0
-1
-2
-3
Percent of Swing Phase
Extensor
Flexor
B.
Average Hip Muscle Torque (mNm/kg)
30
15
0
-15
Average Knee Muscle Torque (mNm/kg)
-10
-20
-30
Average Ankle Muscle Torque (mNm/kg)
0.0
-0.6
-1.2
*
Control
Day 2
Day 6
Day 10
Day 0
Day 1
Days with Weight On
Days after Weight Off

swing phase was significant on Day 2 and Day 10 with the weight on (Fig. 5.12*B*). The fact that knee flexor muscle torque was increased at all during the initial half of the swing phase is surprising since the Pb and ST muscles were denervated. However, from the EMG records, it can be seen that other muscles, which could have knee flexor action (SartM and MG), were recruited to compensate for this deficit. Ankle flexor muscle torque also tended to be greater when the weight was on, particularly on Day 6 with the weight on (which corresponds to the day when the animal made the fewest errors in obstacle clearance (Fig. 5.6). The fact that ankle muscle torque did not become more extensor over the first half of the swing phase suggests that the additional recruitment of MG muscle activity at this time (Fig. 5.11) was primarily used to generate additional knee flexor activity. Hip muscle torque became more extensor during the first half of the swing phase, particularly by Day 10 with the weight on ($p < 0.01$, Fig. 5.12*B*).

When the weight was removed, hip muscle torque tended to be more flexor than control while knee flexor muscle torque was lower than that during control steps (significantly lower on Day 1 after removal of the weight, $p < 0.01$, Fig. 5.12*B*). Again, this was not surprising given the denervation of the Pb and ST muscles. Ankle muscle torque was quite variable but tended to be somewhat more flexor than control values.

5.4 Discussion

The main objective of this study was to investigate the adaptive strategies used by intact cats to step over an obstacle with additional load on their hindlimb. All results were obtained from normal walking cats. In the first experiment, the recording hindlimb was intact except for neurectomy of cutaneous nerves supplying the skin around the shank. The common observation from both cats was evidence for long-term adaptation (learning) to the additional weight. Evidence for this was provided by the fact that after-effects in the locomotor pattern were observed after removal of the weight. One of the cats also exhibited evidence for an immediate adaptive response to the weight, given by the observation that there was high stepping as soon as the weight was added (*cat 1*). The main strategy utilized by both cats was an increase in recruitment of knee flexor activity, corresponding with an increase in ST or SartM muscle activity. This observation led to the second set of experiments where cats underwent an additional procedure to denervate the Pb and ST muscles. When this was done, the cats had difficulty stepping over the obstacle without contacting it (contact with the obstacle never occurred in cats without PbST neurectomy). Regardless of the deficit in knee flexion due to PbST neurectomy, the cat could still learn to step over the obstacle with the weight on, as indicated by the fact that after-effects were observed after removal of the weight.

5.4.1 Methodological Considerations

Since cats were freely walking along a horizontal platform, there was no attempt to control walking speed. *Cat 1* tended to walk about 0.30 m/s faster than the other 2 cats (Table 5.1). Regardless of the differences in walking speed, the analyses focused on comparisons made within each animal. Furthermore, there was no significant difference in walking velocity between stepping conditions with the weight off and weight on in each cat (see Table 5.1). Thus, we felt that normalizing the time scale of the data for comparing stepping conditions within each cat was a valid method. In addition, a comparison of joint angle values for stepping over the obstacle was comparable to those reported previously (see Lavoie et al. 1995; McFadyen et al. 1999).

Our inability to digitize the video data at rates higher than 30 Hz may also have limited the precision of subsequent kinematic and dynamic calculations. We attempted to maximize the data collected, however, by ensuring adequate smoothing of the data before splining the raw data. Visual inspection of the splined data compared with the raw data helped to verify that the splined data points closely followed the movement trajectory. Furthermore, comparison of the data presented here with that from previous kinematic analysis of cats stepping over obstacles using a digitization rate of 60 Hz (McFadyen et al. 1999) yielded very similar results despite possible effects due to differences in individual cats and walking speed.

The analysis in this study focused only on activity of the limb during the swing phase of locomotion since the added weight would produce a main effect during this period. However, we cannot discount any postural modifications that may have occurred in preparation for paw clearance against a heavier weight. Indeed, previous investigations have revealed anticipatory adaptive mechanisms during the support phase in preparation for stepping over an obstacle (Lavoie et al. 1995) and it is possible that some of these anticipatory mechanisms were altered in preparation for paw lift-off with the additional weight. Lavoie et al. (1995) observed that before paw lift-off, increases in vertical ground reaction force with an accompanying increase in extensor muscle activity occurred in the limb that was about to step over the obstacle. It was thought that the purpose of the increase in vertical force helped to propel the body forward as well as raise the body to facilitate clearance of the hindlimb that was about to step over the obstacle (Lavoie et al.

1995). Some indication of this in the present results was provided by an observation that RF activity during late-stance was elevated during leading steps over the obstacle (data not shown). In addition, in figure 5.7C, a general elevation of the experimental leg was shown that corresponded with an increase in paw trajectory height when the weight was on in *cat* 3. Since there was no corresponding change in hip, knee, or ankle joint flexion with the increase in paw trajectory height, the heightened elevation of the limb (as indicated by a higher hip marker position throughout the swing phase) may have served to help clear the obstacle with the weight on. Further experiments with more EMG recordings from both flexor and extensor muscles in *both* hindlimbs are indicated to further understand the adaptive mechanisms that occur before paw lift-off to help clear the weighted limb over the obstacle.

5.4.2 Knee Flexor Activity Plays an Integral Role in the Adaptive Response to Additional Loading of the Limb during Obstacle Avoidance

Animals constantly experience changes in the properties of their limbs throughout a lifetime, whether it is due to growth and development, or injury. The results presented in the first part of this study showed that the main adaptive strategy to the extra load on the leg during obstacle avoidance was an increase in knee flexion, usually associated with an increase in ST or SartM amplitude while stepping over the obstacle. Increases in hip or ankle flexion were also observed, but to a lesser degree and not as consistently between the 2 animals. The emergence of mainly a knee flexor strategy may be attributed to the placement of the additional weight around the shank. The knee, being the nearest proximal joint to the extra weight, is in an optimal position to respond best to the extra weight. In addition, the specific task under study (stepping over obstacles) requires the greatest change to knee mechanics (Lavoie et al. 1995). Lavoie et al. (1995) reported that when the locomotor pattern is adapted from level walking to stepping over obstacles, the main strategies at the forelimb is an increase in flexion of the elbow and at the hindlimb, an increase in knee flexion. In the hindlimbs, McFadyen et al. (1999) also reported that the increase in knee flexion angle was accompanied by an increase in knee flexor muscle power and ST activity during the swing phase. Similarly, during obstacle avoidance in human walking, there is a switch to a predominant knee flexor strategy from the usual hip flexor strategy seen during unobstructed walking (McFadyen and Winter 1991). Moreover, the main strategy to emerge from modeling studies of locomotor adjustments during obstacle avoidance was also an increase in the recruitment of knee flexor activity (McFadyen et al. 1994; Taga 1998). The present results indicate that this adaptive strategy is augmented further to ensure clearance over the obstacle with additional weight on the leg. Significant increases in either the ST or the SartM muscles, which have knee flexor action, were always observed in both cats and in both trailing and leading limbs over the obstacle (data not shown for leading steps). Increases in the amplitude of the IP or SartA muscles, which have flexor action at the hip, were also observed, but they were never statistically significant except during the first few days with the weight on during trailing steps over the obstacle in *cat 1*. Furthermore, denervation of the Pb and ST muscles, thus rendering them unable to generate force or respond to changes in proprioceptive input, severely diminished the ability of the animal to clear the obstacle with the additional weight (Fig. 5.6). Despite the deficit induced by the PbST nerve cut in *cat 3*, additional strategies emerged that compensated for the weakness in knee flexor action. Most interesting was the recruitment of MG activity when the weight was on during the flexor phase of walking which, together with elevated SartM activity, was associated with greater knee flexor muscle torque.

Another aspect of the role of the knee flexors PbST and gracilis muscles during obstacle avoidance emerged from *experiment 2*. In *cat 3*, even after the weight was removed, the slope of the initial rise of paw trajectory, after any after-effects disappeared (Days 1-2 after weight off), remained lower than control levels (Fig. 5.7 and 5.10). Furthermore, there were some errors, although little in number, which were committed even after the weight was removed and which could be attributed to the loss of activity in the Pb, ST, and gracilis. A recent report by Yakovenko et al. (2002) argues for the idea that the hamstrings muscles (including ST, Pb, semimembranosus) as well as gracilis and the toe flexor, flexor digitorum longus (FDL) form a functional muscle group (the 'retractors') that work in concert to complete propulsive action of the leg during late-stance and produce the initial rise in paw trajectory during early swing. Thus, the persistent deficit in the initial slope of the paw trajectory after any after-effects disappeared when the weight was removed could be attributed to loss of contribution from the Pb, ST, and gracilis muscles in *cat 3*. This functional role of the hamstrings, gracilis, and FDL could also account for the finding that while leading steps over the obstacle recovered error-free clearance of the obstacle very quickly, the time-line for recovery during the trailing steps over the obstacle was more protracted and was incomplete in *cat 3*. During trailing steps over the obstacle, the limb is in a more extended position, particularly at the hip, compared with leading steps at the time of paw lift-off (Fig. 5.5A). In this position, extension of the hip in conjunction with knee flexion may be important for raising the limb in preparation for clearance. Indeed, the onset of ST activity is earlier during trailing steps over the obstacle compared with leading steps

(Fig. 5.5*B*; also see McFadyen et al. 1999). During leading steps over the obstacle, the hip is in a relatively more flexed position at the time of paw lift-off (Fig. 5.5A) and hip flexor muscles may be more important for ensuring clearance over the obstacle during these steps (Fig. 5.5*B*). This idea is supported by McFadyen et al. (1999) who show greater hip flexor muscle torque and power at the beginning of the swing phase during leading steps over the obstacle compared with trailing steps (also cf. Fig. 5.9B and 5.12B, *Average Hip Muscle Torque*). Thus, removal of input from Pb, ST, and gracilis (3 of the 'retractor' muscles) (Yakovenko et al. 2002) could account for the greater deficit in obstacle avoidance during trailing steps over the obstacle compared with leading steps.

5.4.3 Implications of After-Effects – Was There Learning?

In non-rhythmic motor systems controlling discrete movements (such as reaching), adaptation, or learning of new skills is often discussed in terms of a recalibration or adjustment of the motor program generating the output for a specific task (reviewed in Kawato 1999). Typically, unexpected removal of the perturbing input reveals the presence of this recalibration in the form of an after-effect. After-effects were observed in the present study as high stepping after removal of the weight, usually accompanied by persistent increases in knee flexor muscles and sometimes in the hip flexor IP. The persistent elevation of flexor muscle activity is consistent with the idea that there was a reconfiguration in flexor-generating mechanisms of the locomotor system. In the cat with PbST neurectomy, investigation of the torque profiles after the weight was removed demonstrated a persistent increase in hip and ankle flexor muscle torque at the beginning of swing. This suggests that hip and ankle strategies used to adapt to the additional weight were more long lasting in nature, possibly involving a reconfiguration of the mechanisms producing hip and ankle motor output during locomotion.

What were the sensory signals that triggered and mediated the response to additional weight on the hindlimb and where was the site of this adaptation? One likely source of sensory input was the loading of the flexor muscles when the additional weight was added. Previous results from decerebrate walking cats have shown that hip flexor muscle activity during the swing phase of locomotion increases in response to proprioceptive disturbances that resist forward movement of the limb (Lam and Pearson 2001). This response is likely mediated by hip flexor muscle afferents that signal load and length changes (see Chapter 4). The addition of 100 grams of weight, which effectively doubles the mass of the shank, would similarly load the flexor muscles as the limb is raised upwards and forwards through the swing phase. Thus, inputs from load- and length-sensitive muscle afferents are possible signals that mediate the learning of obstacle avoidance with the weight on. Evidence for learning was also obtained in cats with denervation of the Pb and ST muscles. In addition to feedback due to the additional weight on the limb, error signals due to contact of the paw with the obstacle in these cats are likely another source of afferent input that could trigger and mediate adaptations with the weight on. Specifically, contact of the paw with the obstacle would activate stretch-sensitive muscle afferents, particularly in ankle flexor muscles. Activation of muscle afferents in this way might then eventually initiate greater production of flexor activity in the following steps in order to avoid contact with the obstacle. Cutaneous signals did not likely play a major role in triggering the adaptive responses in these cats since the nerves supplying the skin of the shank and paw were denervated.

Signals from muscle afferents could have mediated both the immediate and the long-term adaptive responses via their reflex pathways to flexor motoneurons. In the extensor generating system during locomotion, adjustments to the gain of spinal reflex pathways are involved in adapting extensor muscle activity in response to ankle extensor neurectomy (Whelan and Pearson 1997; Pearson et al. 1999; Pearson and Misiaszek 2000). A similar mechanism could have been involved in mediating the increases in hip or knee flexor muscle activity when the weight was on in the present experiments. Indeed, flexor motoneurons receive excitatory feedback from homologous load- and length-sensitive muscle afferents (Perreault et al. 1995; Degtyarenko et al. 1998; McCrea et al. 2000; Quevedo et al. 2000). Thus, it is possible that an increase in gain in these reflex pathways in response to the additional loading on the hindlimb was involved in the adaptive increase in flexor activity when the weight was on. Proprioceptive feedback pathways could also play a role in immediate adaptive responses (those that do not entail long-lasting changes in locomotor-generating networks). Such short-term adaptive responses might have produced the immediate high stepping seen in *cat 1* on the same day that the weight was added. They also could have mediated the adaptive knee flexor response during leading steps over the obstacle in *cat 3*. In this case, elevated knee flexor muscle torques when the weight was on did not persist after removal of the weight while increases in hip and ankle flexor muscle torques were maintained after the weight was removed (Fig. 5.9). The fact that an after-effect, in terms of a persistent elevation of knee flexor muscle torque, was not observed suggests that this strategy was a moment-by-moment adjustment to the locomotor program and was not incorporated into a long-term adaptive learning strategy to the additional weight on the hindlimb.

Structures and pathways in the cerebellum are other potential candidates that could have been involved in mediating the adaptive responses to the additional weight on the hindlimb. The cerebellum has been shown to be involved during motor learning in many motor tasks (Gomi et al. 1998; Thach 1998; Kawato 1999; Imamizu et al. 2000). During locomotion, inactivation of nitric oxide pathways in the cerebellum was shown to prevent the ability of decerebrate cats to adapt to a split-belt treadmill (Yanagihara and Kondo 1996). Humans with cerebellar lesions also show deficits in the adaptation to speed perturbations during walking (Rand et al. 1998). In addition, spinal inputs to the cerebellum are organized in such a way that would provide a framework for an involvement in locomotor adaptations. Proprioceptive inputs from the hindlimb are directly conveyed to the cerebellum via dorsal spinocerebellar tracts (DSCT). These neurons receive convergent input from a wide variety of sensory receptors, including muscle sensory receptors, from the hindlimb and respond to global changes in hindlimb position (end-point position and joint angles) (Bosco et al. 2000b; Poppele et al. 2002). Although these observations were obtained from anesthetized cats, combining passive hindlimb movements with electrical muscle stimulation further supported the kinematic basis of information carried via the DSCT (Bosco and Poppele 2000a). Additionally, neurons of the DSCT are active during locomotion (Arshavsky et al. 1972). Thus, it is possible that information carried by the DSCT signaled changes (or errors) in the kinematic parameters of the cat hindlimb during walking with the additional weight on, thereby initiating adaptive changes to the locomotor pattern by adjusting muscle activation patterns (and joint torques) to match the desired limb positions (Bosco and Poppele 2001). Given the involvement of the motor cortex during the swing phase of walking (Drew et al. 1996), it is also possible that changes in descending drive from the cortex to locomotor centres in the spinal cord was involved in adapting to the additional weight. Such changes in descending drive could have mediated adaptive changes during locomotion by a direct influence on spinal locomotor centres (e.g. as indicated by Carrier et al. 1997 and Gritsenko et al. 2000), or by increasing the gain in proprioceptive feedback pathways (e.g. as indicated by Wolpaw 1997 and Chen et al. 2002).

5.4.4 Conclusions

This study has described the long-term adaptive strategies used by cats during obstacle avoidance with additional load on the hindlimb. A consistent strategy used by the 2 cats involved an augmentation of knee flexor activity in order to clear the obstacle with the additional weight. Evidence for both immediate adaptation (immediate high stepping after addition of the weight) as well as more long-lasting learning effects (persistent after-effects after removal of the weight) were obtained in response to the extra weight. The capacity for adaptation is also retained despite denervation of knee flexor muscles. In this cat, hip, knee, and ankle flexor strategies were used to compensate for the additional weight on the leg. However, examination of the steps that showed an after-effect after removal of the weight revealed that only the elevation in hip and ankle flexor muscle torque persisted.

5.5 References

Anstis S. Aftereffects from jogging. *Experimental Brain Research* 103: 476-478, 1995.

Arshavsky YI, Berkinblit MB, Fukson OI, Gelfand IIM, Orlovsky N. Recordings of neurons of the dorsal spinocerebellar tract during evoked locomotion. *Brain Research* 43: 272-275, 1972.

Beloozerova IN, Sirota MG. The role of the motor cortex in the control of accuracy of locomotor movements in the cat. *Journal of Physiology* 461: 1-25, 1993.

Bosco G, Poppele RE. Reference frames for spinal proprioception: kinematics based or kinetics based? *Journal of Neurophysiology* 83: 2946-2955, 2000a.

Bosco G, Poppele RE. Proprioception from a spinocerebellar perspective. *Physiological Reviews* 82: 539-568, 2001.

Bosco G, Poppele RE, Eian J. Reference frames for spinal proprioception: limb endpoint based or joint-level based? *Journal of Neurophysiology* 83: 2931-2945, 2000b.

Carrier L, Brustein E, Rossignol S. Locomotion of the hindlimbs after neurectomy of ankle flexors in intact and spinal cats: model for the study of locomotor plasticity. *Journal of Neurophysiology* 77: 1979-1993, 1997.

Chen XY, Carp JS, Chen L, Wolpaw JR. Corticospinal tract transection prevents operantly conditioned H-reflex increase in rat. *Experimental Brain Research* 144: 88-94, 2002.

Degtyarenko AM, Simon ES, Norden-Krichmar T, Burke RE. Modulation of oligosynaptic cutaneous and muscle afferent reflex pathways during fictive locomotion and scratching in the cat. *Journal of Neurophysiology* 79: 447-463, 1998.

Drew T, Jiang W, Kably B, Lavoie S. Role of the motor cortex in the control of visually triggered gait modifications. *Canadian Journal of Physiology and Pharmacology* 74: 426-442, 1996.

Duysens J, Clarac F, Cruse H. Load-regulating mechanisms in gait and posture: comparative aspects. *Physiological Reviews* 80: 83-133, 2000.

Gomi H, Shidara M, Takemura A, Inoue Y, Kawano K, Kawato M. Temporal firing patterns of Purkinje cells in the cerebellar ventral paraflocculus during ocular following responses in monkeys. I. Simple spikes. *Journal of Neurophysiology* 80: 818-831, 1998.

Gordon CR, Fletcher WA, Jones GM, Block EW. Adaptive plasticity in the control of locomotor trajectory. *Experimental Brain Research* 102: 540-545, 1995.

Gritsenko V, Mushahwar V, Prochazka A. Adaptive changes in locomotor control after partial denervation of triceps surae muscles in the cat. *Journal of Physiology* 533: 299-311, 2000.

Hoy MG, Zernicke RF. Modulation of limb dynamics in the swing phase of locomotion. *Journal of Biomechanics* 18: 49-60, 1985.

Hoy MG, Zernicke RF. The role of intersegmental dynamics during rapid limb oscillations. *Journal of Biomechanics* 19: 867-877, 1986.

Imamizu H, Miyauchi S, Tamada T, Sasaki Y, Takino R, Pütz B, Yoshioka T, Kawato M. Human cerebellar activity reflecting an acquired internal model of a new tool *Nature* 403: 192-195, 2000.

Kably B, Drew T. Corticoreticular pathways in the cat. II. Discharge activity of neurons in area 4 during voluntary gait modifications. *Journal of Neurophysiology* 80: 406-424, 1998.

Kawato M. Internal models for motor control and trajectory planning. *Current Opinion in Neurobiology* 9: 718-727, 1999.

Lam T, Pearson KG. Proprioceptive modulation of hip flexor activity during the swing phase of locomotion in decerebrate cats. *Journal of Neurophysiology* 86: 1321-1332, 2001.

Lavoie S, McFadyen B, Drew T. A kinematic and kinetic analysis of locomotion during voluntary gait modification in the cat. *Experimental Brain Research* 106: 39-56, 1995.

Lou J-S, Bloedel JR. A new conditioning paradigm: conditioned limb movements in locomoting decerebrate ferrets. *Neuroscience Letters* 84: 185-190, 1988.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233, 2000.

McFadyen BJ, Winter DA. Anticipatory locomotor adjustments during obstructed human walking. *Neuroscience Research Communications* 9: 37-44, 1991.

McFadyen BJ, Lavoie S, Drew T. Kinetic and energetic patterns for hindlimb obstacle avoidance during cat locomotion. *Experimental Brain Research* 125: 502-510, 1999.

McFadyen BJ, Winter DA, Allard F. Simulated control of unilateral, anticipatory locomotor adjustments during obstructed gait. *Biological Cybernetics* 72: 151-160, 1994.

Misiaszek JE, Pearson KG. Adaptive changes in locomotor activity following botulinum toxin injection in ankle extensor muscles of cats. *Journal of Neurophysiology* 87: 229-239, 2002.

Pearson KG. Proprioceptive regulation of locomotion. *Current Opinion in Neurobiology* 5: 786-791, 1995.

Pearson KG, Fouad K, Misiaszek JE. Adaptive changes in motor activity associated with functional recovery following muscle denervation in walking cats. *Journal of Neurophysiology* 82: 370-381, 1999.

Pearson KG, Misiaszek JE. Use-dependent gain change in the reflex contribution to extensor activity in walking cats. *Brain Research* 883: 131-134, 2000.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Poppele RE, Bosco G, Rankin AM. Independent representation of limb axis length and orientation in spinocerebellar response components. *Journal of Neurophysiology* 87: 409-422, 2002.

Prentice SD, Drew T. Contributions of the reticulospinal system to the postural adjustments occurring during voluntary gait modifications. *Journal of Neurophysiology* 85: 679-698, 2001.

Prokop T, Berger W, Zijlstra W, Dietz V. Adaptational and learning processes during human split-belt locomotion: interaction between central mechanisms and afferent input. *Experimental Brain Research* 106: 449-456, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Rand MK, Wunderlich DA, Martin PE, Stelmach GE, Bloedel JR. Adaptive changes in responses to repeated locomotor perturbations in cerebellar patients. *Experimental Brain Research* 122: 31-43, 1998.

Rossignol S. Neural control of stereotypic limb movements. In: *Handbook of Physiology, Section 12: Exercise : Regulation and Integration of Multiple Systems,* edited by LB Rowell and JT Shepherd. New York, NY: American Physiological Society by Oxford University Press, 1996, pp. 173-216.

Taga G. A model of the neuro-musculo-skeletal system for anticipatory adjustment of human locomotion during obstacle avoidance. *Biological Cybernetics* 78: 9-17, 1998.

Thach WT. A role for the cerebellum in learning movement coordination. *Neurobiology of Learning and Memory* 70: 177-188, 1998.

Weber KD, Fletcher WA, Gordon CR, Jones MG, Block EW. Motor learning in the "podokinetic" system and its role during spatial orientation during locomotion. *Experimental Brain Research* 120: 377-385, 1998.

Whelan PJ, Hiebert GW, Pearson KG. Plasticity of the extensor group I pathway controlling the stance to swing transition in the cat. *Journal of Neurophysiology* 74: 2782-2787, 1995.

Whelan PJ, Pearson KG. Plasticity in reflex pathways controlling stepping in the cat. *Journal of Neurophysiology* 78: 1643-1650, 1997.

Widajewicz W, Kably B, Drew T. Motor cortical activity during voluntary gait modifications in the cat. II. Cells related to the hindlimbs. *Journal of Neurophysiology* 72: 2070-2089, 1994.

Wolpaw JR. The complex structure of a simple memory. *Trends in Neurosciences* 20: 588-594, 1997.

Yakovenko S, Mushahwar V, VanderHorst V, Holstege G, Prochazka A. Spatiotemporal activation of lumbosacral motoneurons in the locomotor step cycle. *Journal of Neurophysiology* 87: 1542-1553, 2002.

Yanagihara D, Kondo I. Nitric oxide plays a key role in adaptive control of locomotion in cat. *Proceedings of the National Academy of Science USA* 93: 13292-13297, 1996.

Zehr EP, Stein RB. What functions do reflexes serve during human locomotion? *Progress in Neurobiology* 58: 185-205, 1999.

CHAPTER 6

HOW DO INFANTS ADAPT TO LOADING OF THE LIMB DURING THE SWING PHASE OF STEPPING?

Adapted from an original manuscript:
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6.1 Introduction

Human infants show a stepping response that is sensitive to transient changes in sensory input (Yang et al. 1998a, 1998b; Pang and Yang 2000, 2001). In this study, we investigated whether infants have the capacity for adapting to sustained changes in sensory input during stepping. Adult humans and other mammals make adaptive modifications after injury or sustained changes in sensory input (Pearson 2000). Changes in the gain of spinal reflex pathways, changes in drive from locomotor generating networks, and input from supraspinal centres have all been shown to be involved in mediating these adaptive responses to the locomotor pattern after peripheral nerve injury (Carrier et al. 1997; Whelan and Pearson 1997; Pearson et al. 1999; Pearson and Misiaszek 2000; Gritsenko et al. 2001).

Some studies have also examined adaptive changes to locomotion that are not induced by nerve injury. In these types of studies, compensations are seen not only in the presence of the perturbation, but long-term adaptive strategies are revealed upon the removal of the perturbation from the locomotor environment. For example, decerebrate ferrets adaptively increased the trajectory of their forelimb in order to avoid a rod placed in the forelimb's path. When the rod was removed, high stepping continued for up to 7 steps before the stepping pattern returned to control trajectories (Lou and Bloedel 1988). Thus, in the presence of the obstacle, mechanisms were employed to generate the higher stepping to prevent contact with the obstacle. When the obstacle was removed, the persistent high stepping (after-effect) indicated that these adaptive mechanisms involved feedforward control that anticipated the presence of the obstacle. In humans, analogous experimental results have indicated that feedforward control mechanisms are also employed to adapt to changes in sensory input. Rather than using specific proprioceptive disturbances, the perturbations to locomotion in these cases were more global, involving inter-limb coordination (Gordon et al. 1995; Jensen et al. 1998; Weber et al. 1998) or locomotor speed (Anstis 1995). Nevertheless, the presence of after-effects after removal of the perturbing input indicates the role of feedforward mechanisms to adapt to the initial disturbances.

Is the ability to adapt to sustained changes in the biomechanical properties of the body present in the human locomotor system *before* independent walking develops? In an attempt to answer this question, this study focused on the swing phase of stepping and examines how infants respond and adapt to a change in the amount of load on their leg. Two specific questions were addressed. First, can infants adapt (as seen by an after-effect) to a sustained change in proprioceptive input during treadmill stepping? Second, if they are able to adapt, what is the nature of the strategies used to achieve the adaptation? These data were previously presented in abstract form (Yang and Lam 2001).

6.2 Methods

6.2.1 *Subjects and Preparation*

Twenty-two infants between the ages of 3 and 11 months and ranging in weight from 5.7 to 11.6 kg were recruited from local public health clinics. Parents/guardians gave voluntary and written consent on behalf of their infant for participation in the study. All procedures were conducted in accordance with the ethical guidelines of the University of Alberta and the local health authority. One month before the recording session, parents were given verbal instruction on methods to practice the stepping response with their infant as described in Yang et al. (1998a). This helped to ensure that the stepping response could be elicited on the day of the recording session especially in infants who were younger than 7 months.

Adhesive joint markers were taped to the skin overlying the following bony landmarks on the left leg: the superior border of the iliac crest, the greater trochanter of the femur, the knee joint line, the lateral malleolus, and the head of the fifth metatarsal. The lengths of the thigh, lower leg, and foot were measured by hand using a standard tape measure. The mass of the infant was also measured for subsequent anthropometric calculations used in the inverse dynamic calculations (Schneider et al. 1990).

Stepping was elicited by holding the infant under the arms and allowing the feet to touch a slowly moving treadmill belt (0.2 to 0.3 m/s). The stepping was recorded from the left side with a video camera at 30 frames/second. After a period of undisturbed (control) stepping, a small weight (500 to 900 g, depending on the infant's size) made from stretchable cloth and filled with ball bearings was strapped around the left lower leg. Stepping with the weight on was elicited for a period of 30 seconds to 2 minutes, depending on the infant's tolerance. After this period, the weight was rapidly detached from the limb while the infant was stepping. Care was taken to remove the weight as quickly as possible while minimizing disruption to the ongoing stepping sequence. Stepping was allowed to continue for at least 30 seconds after the weight was detached. This sequence (control stepping, weight on, weight off) was usually performed once for each infant. In 3 infants, this sequence was repeated twice and in 1 infant, the sequence was repeated 4 times to examine the consistency within subjects of the response to the weight.

6.2.2 Data Analysis

We focused our analysis on kinematic and kinetic measures of movement during the swing phase of stepping because the load was applied such that the main effect would be during the swing phase. Furthermore, flexor muscle activity at the knee and hip are difficult to record by surface electromyography in infants given the small size of the legs, the deep location of the muscles (particularly hip flexor muscles), and fatty tissue in these areas. Since our study focused on the swing phase, a measure of flexor activity at these joints is crucial to our analysis and we felt kinetic analysis would provide the best solution.

The data were divided into 3 sections: control, weight on, and weight off stepping. The selected video data were then digitized from the videotape to the computer at 30 Hz using Adobe Premiere (Adobe Systems Inc., San Jose, CA). The positions of the joint markers were then digitized by hand using custom-written software.

Subsequent analysis was performed using custom software written with MATLAB (MathWorks, Natick, MA). The position data of the trunk, hip, knee, ankle, and toe were filtered using a 4th-order Butterworth, dual-pass filter. The low-pass cut-off frequency was set to 6 Hz. The velocity and acceleration of the hip, knee, and ankle joints were then calculated by derivative technique.

Ten control steps were randomly chosen to provide baseline measures of the kinematics of infant stepping. Pilot data indicated that a minimum of 10 steps would provide an adequate measure of normal, undisturbed infant stepping (data not shown). To measure the effect of adding the extra weight to the leg, the first and last 3 steps taken with the weight on were chosen for full kinematic and kinetic analysis. The initial steps with the weight on were also of particular importance since an immediate increase in flexor activity due to the extra weight may indicate mechanisms mediated by spinal or brainstem reflex pathways. To gauge whether there was a time-dependent adaptation to the weight, the maximum toe height was measured from all the steps taken (to a maximum of 40) with the weight on.

Any after-effect (high stepping) that might arise upon removal of the weight was gauged by the maximum height in the trajectory of the toe achieved in the first step taken when the weight was removed. A one-tailed z-test was used to determine significant increases in toe trajectory height above the mean of control steps ($p < 0.05$). We thus attempted to group infants according to whether they showed an after-effect or not, as measured by these values (Fig. 6.1).

Infant treadmill stepping is not as regular or consistent as adult stepping. Often, there is out-of-plane movement due to variable movements, usually external rotation of the leg during swing. To determine the extent of out-of-plane movement, the apparent lengths of the thigh, leg, and foot were measured. If the length varied by more than 10%, the data set was not used in the analysis. If the apparent length varied within the acceptable range, inverse dynamic analysis was performed to calculate the torques (muscle, gravitational, and interaction) at the hip, knee, and ankle (Hoy and Zernicke 1986; see also Appendix 1). Thigh and leg movements were rarely out of plane. If they were, data from that step were discarded (n = 14 steps discarded). Foot movement was often out of plane. In these situations, 2-segment analysis (where the foot and shank were considered as one segment) was applied which did not require input from kinematic values from the foot. Out of all the infants tested and steps chosen for the complete kinematic and kinetic analysis (462 steps), we used 2-segment analysis for 110 steps due to out-of-plane movement at the foot. In any case, contribution from forces at the ankle were very small (data not shown), especially considering the relatively small mass of the foot (less than 1% of body mass and less than 10% of total leg mass) (Schneider et al. 1990). Furthermore, there was little significant change in ankle torques during the different stepping conditions, probably because the weight was strapped to the lower leg and did not load the foot. Thus, separate results from the ankle torque calculations will not be presented in this paper. Due to the range of body weights across individual infants, all torque values from each infant were normalized to the infant's body mass (Winter 1991).

The swing phase was divided into 2 equal parts using the following terminology: the first half, or early swing and the last half, or late swing. For each condition, the average muscle torque during the first half of swing was calculated. This gave an indication of the muscle activity produced to promote clearance of the foot. Muscle torque produced during the last half of swing mainly slows the limb in preparation for ground contact. Since muscle activity produced during early swing would be most affected by the unexpected removal of the weight, we focused on this part of the swing phase although torque profiles for the complete duration of the swing phase are presented.

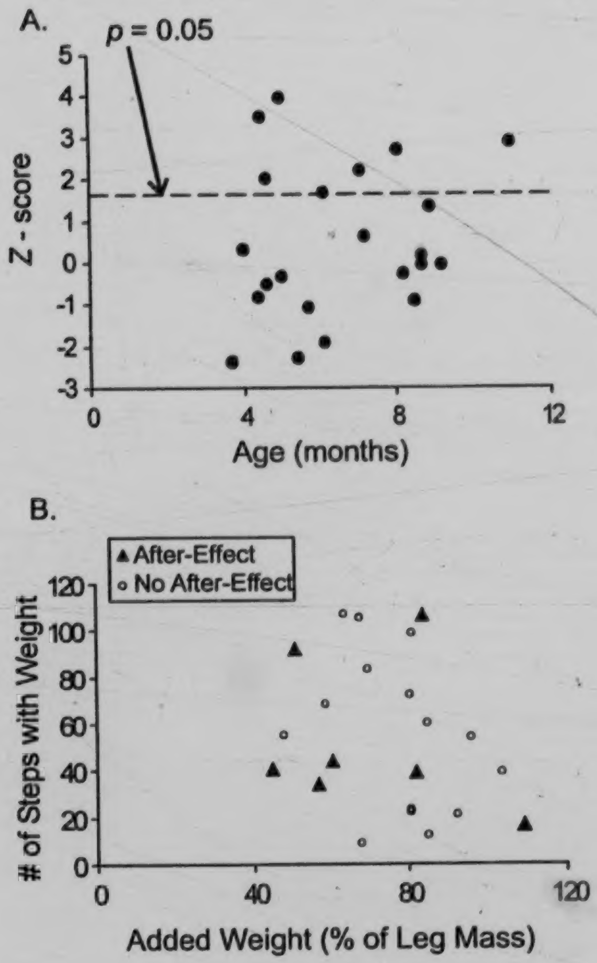
6.3 Results

The objectives of this study were to examine whether infants could adapt to an extra load on their leg during stepping and if they could, how this adaptation was achieved. To address the issue of whether learning had occurred, we measured the maximum height of the toe trajectory in the first step with the weight off. Figure 6.1A illustrates this measure for all infants tested. Each point in the graph represents one infant. For each infant, the difference in maximum toe trajectory height between averaged control steps and the first step with the weight off is expressed as a *z*-score and plotted along the y-axis. The infant's age is plotted along the x-axis. The dashed line in the graph delineates a *z*-score value of 1.645, which corresponds with a p value of 0.05 (one-tailed *z*-test). Infants were thus categorized into one of 2 groups, those that showed an after-effect (corresponding with a significantly higher ($p < 0.05$) toe trajectory in the first step with the weight off) ($n = 7$) and those that did not show an after-effect ($n = 15$). Note that there was no clear relationship between the presence of an after-effect and the age of the infant. Of the infants who did not show an after-effect, 3 showed a significantly lower toe trajectory in the first step with the weight off (z-score < -1.645). The significance of this finding is unclear but may represent an alteration in the general state of the infant, not necessarily associated with the experience with the weight on. However, no discernable change in mood during the course of the experiment was observed in 2 of these infants while one of them was slightly more upset by the end of the experimental session.

A possible explanation for the lack of an after-effect in the majority of the infants tested might be related to the amount of weight applied or the number of steps taken with the weight. We examined this issue in figure 6.1*B*, which is a plot describing the characteristics of the sample of infants used in this study. Each data point in the scatterplot represents one infant. The data were plotted as the number of steps taken with the weight against the amount of weight applied (expressed as a percentage of leg mass). This gives an indication of the amount of exposure to the extra weight (number of steps with weight) and

Figure 6.1. Grouping of Infants - After-Effects and No After-Effects.

A. The change in toe trajectory after the weight was removed compared with control steps expressed as a z score. Each point in the plot represents one infant and the data are arranged by the age of the infant (month). The dashed line delineates a z score of 1.645, which corresponds with $p < 0.05$. *B.* Incidence of after-effects as a function of the amount and intensity of exposure to the extra weight on the leg. Open circles represent infants who did not show after-effects (n = 15). Filled triangles represent infants who did show after-effects (n = 7). Neither the number of steps taken with the weight on nor the amount of extra weight relative to the mass of the infant's leg appeared to be related to the presence of an after-effect.


A.
p = 0.05
Z - score
5
4
3
2
1
0
-1
-2
-3
0
4
8
12
Age (months)
B.
▲ After-Effect
○ No After-Effect
# of Steps with Weight
120
100
80
60
40
20
0
0
40
80
120
Added Weight (% of Leg Mass)

the intensity of the exposure (mass of weight). Infants were grouped according to whether they showed an after-effect (filled triangle symbols) or not (open circle symbols). The amount or intensity of the exposure to the extra weight did not seem to have an influence on whether an after-effect was seen. The infants who showed an after-effect had a range of exposure to the weight, from 20 to more than 100 steps, and a range of weights applied, from 45% to 110% of the mass of the limb.

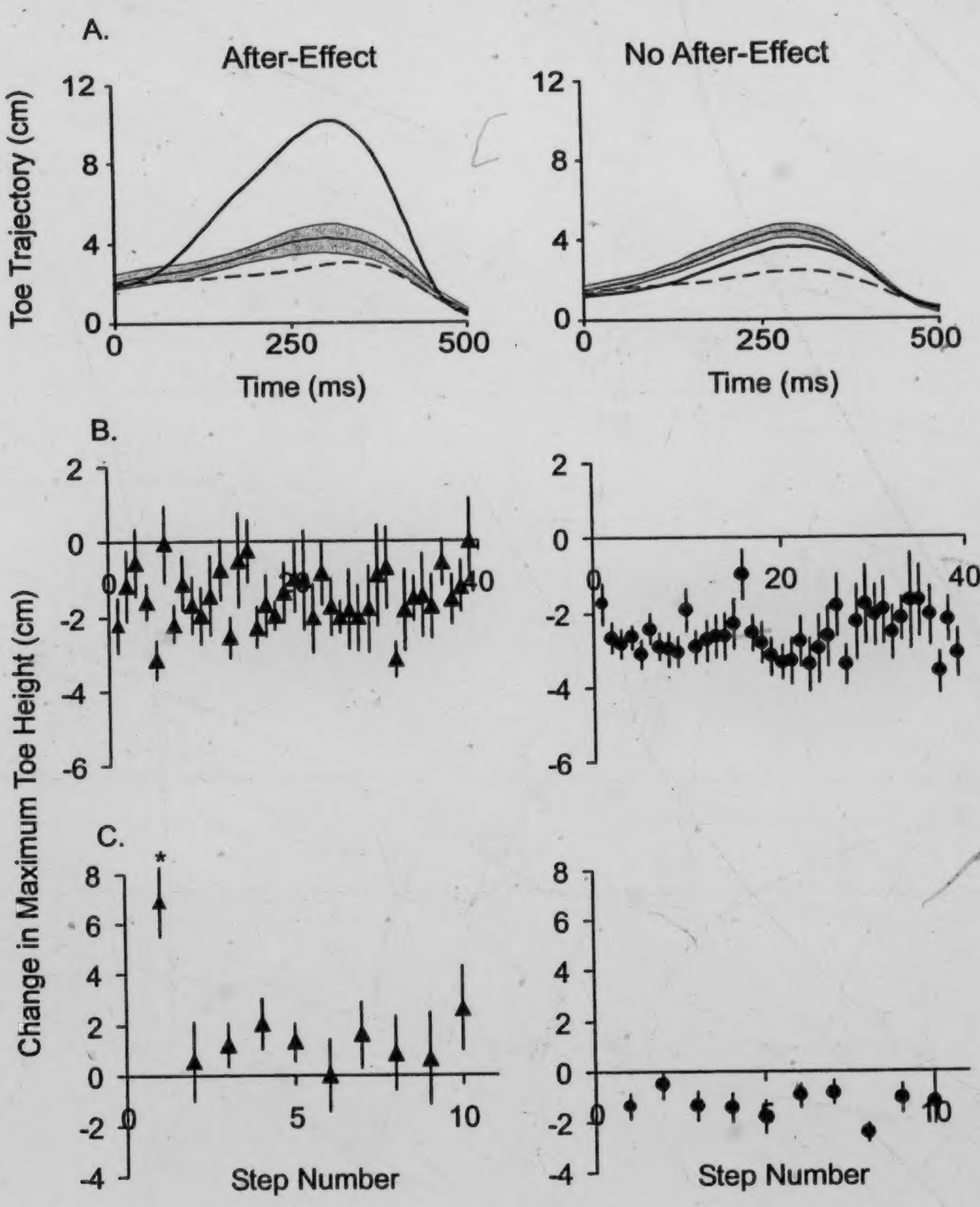
6.3.1 Kinematics

Figure 6.2 shows the toe trajectories during the swing phase from all infants. The data are shown for 2 groups of infants, those who showed an after-effect, and those who did not. In figure 6.2*A*, the thin solid line surrounded by gray shading represent the average and standard error (respectively) of the trajectory of the toe during control steps. Figure 6.2*A* shows that the toe trajectory was consistently lower than control when the weight was on throughout the stepping sequence (dashed black lines). The thick solid line represents the response upon removal of the weight in the 2 groups of infants. In the 7 infants who were categorized in the after-effect group, the high steps taken after the weight was removed is evident in the average toe trajectory of the first step with the weight off (Fig. 6.2*A*, left panel). The high stepping evident in this group of infants is in stark contrast to the return to near control toe trajectory in the other group of infants (Fig. 6.2*A*, right panel).

The maximum toe trajectory height during the swing phase was measured for each step taken with the weight on and off and plotted in figures 6.2*B* and C as a change from control steps of all infants. Each point in the plots represents the average change in

Figure 6.2. Changes in Toe Trajectory with the Weight On and Off.

A. The average toe trajectory of weight on steps (dashed line) and the first step taken after the weight was removed (thick black line). The solid line surrounded by gray shading represents control and standard error, respectively. *B*. The change in maximum toe trajectory height when the weight was on compared to control was calculated for both groups of infants. Each symbol in the plots represents the average change in maximum toe height across all infants in each group (error bars represent standard error). C. The change in maximum toe trajectory height after the weight was removed for both groups of infants. Asterisk (*) represents $p < 0.05$.


A.
After-Effect
No After-Effect
Toe Trajectory (cm)
12
8
4
0
0
250
500
Time (ms)
B.
Change in Maximum Toe Height (cm)
2
0
-2
-4
-6
0
20
40
C.
*
8
6
4
2
0
-2
-4
0
5
10
Step Number

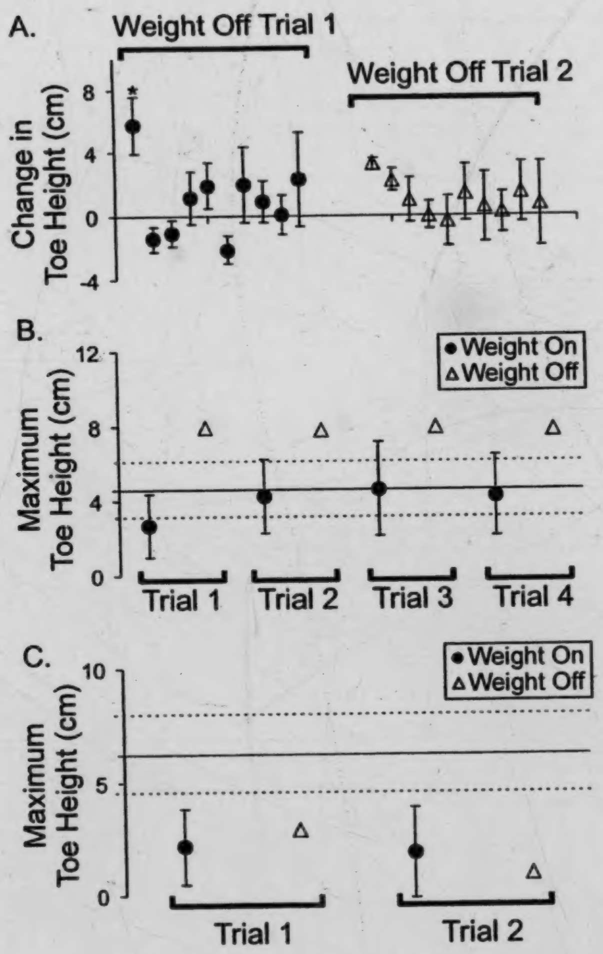
maximum toe trajectory height across the infants in each group (after-effect and no after-effect). If repeated trials were obtained from an infant, only the first trial with the weight on was included in these ensemble plots. Both groups of infants tended to attain lower toe trajectory heights throughout the stepping period with the weight on (Fig. 6.2*B*). However, the group of infants who did not show an after-effect tended to show lower toe trajectory heights throughout compared to the group who did show after-effects. In addition, there was no discernable pattern of adaptation in toe trajectory height during the period with the weight on in either group of infants. There was similarly no apparent time-dependent pattern of adaptation seen in hip or knee flexion during the period with the weight on (data not shown).

When the weight was removed, the maximum toe trajectory height returned to control values in the infants who did not show an after-effect (Fig. 6.2C, right panel). In the other group of infants, maximum toe trajectory height was significantly elevated in the first step after the weight was removed (*t*-test, $p < 0.05$). In subsequent steps, the maximum toe trajectory height tended to remain slightly elevated compared to control levels (Fig. 6.2C, left panel).

In 4 infants, we tested the consistency of the response to sudden removal of the weight by repeating trials of stepping with the weight on at least 2 times. In three of these infants, we observed high stepping after removal of the weight that was consistent for both repeated trials. In one infant, high stepping was not observed after removal of the weight and this was also consistent for both repeated trials. Figure 6.3A shows the average response across 3 infants of successive steps after the weight was removed following the first trial with the weight on (filled circles) and following the second trial with the weight on (open

Figure 6.3. Repeated Trials with the Weight On.

A. Weight off steps after 2 successive repeated trials recorded from 3 infants who showed after-effects. Error bars represent standard error. Asterisks (*) represents $p < 0.05$. *B*. Change in maximum vertical height of the toe trajectory in steps taken with the weight on and after the weight was removed in an infant who showed after-effects after successive trials with the weight on. C. Change in toe trajectory height in steps taken with the weight on and after the weight was removed in an infant who did not show an after-effect. In both *B* and C, the average and standard deviation of the maximum toe trajectory height of control steps are represented by solid and dotted lines, respectively.


A.
Weight Off Trial 1
Weight Off Trial 2
Change in Toe Height (cm)
8
4
0
-4
*
B.
Maximum Toe Height (cm)
12
8
4
0
● Weight On
△ Weight Off
Trial 1
Trial 2
Trial 3
Trial 4
C.
Maximum Toe Height (cm)
10
5
0
● Weight On
△ Weight Off
Trial 1
Trial 2

triangles). In both cases, high stepping was seen in the first step after the weight was removed. After the first trial with the weight on, the height of the toe trajectory was significantly higher than control values in the first step after the weight was removed ($p < 0.05$) in all 3 infants. After the second trial with the weight on, the height of the toe trajectory also tended to be higher than control values although this difference was only significant in one of the 3 infants in this group. The other 2 infants had z-scores of 1.29 and 1.58, which correspond to p-values of 0.09 and 0.06, respectively. Figure 6.3*B* illustrates data from a single infant where repeated trials with the weight on were obtained 4 times (the first 2 trials from this infant were also included in Fig. 6.3A). After the first trial with the weight on (filled circles), the height of the toe trajectory was significantly higher than control levels in the first step after the weight was removed (open triangles). This pattern was observed after each of the subsequent 3 trials with the weight on (Fig. 6.3*B*). Figure 6.3C illustrates data from a single infant where 2 repeated trials with the weight were recorded. After each trial with the weight on, this infant did not show high stepping in the steps immediately following removal of the weight. In fact, the maximum toe trajectory after the weight was removed was significantly lower than control values ($p < 0.05$). This infant was one of the 3 infants who showed a significantly lower toe height after removal of the weight (see Fig. 6.1A). To summarize, in the 4 infants tested in this way, the presence or absence of after-effects after removal of the weight appeared to be consistent across repeated trials.

For each infant, the maximum toe trajectory, maximum hip flexion, and maximum knee flexion was measured for the steps when the weight was on and when the weight was removed and compared to control steps. The group of infants who did show an after-effect appeared to adapt their stepping well to the extra weight on the leg. When the weight was on, there was no overall statistical difference in the average height of the toe trajectory or maximum hip or knee flexion achieved compared to control steps ($p > 0.05$) (Fig. 6.4A, C, E, *Weight On Steps*). When the weight was removed, the height of the toe trajectory, maximum hip flexion, and maximum knee flexion angle in the first step was significantly higher than control ($p < 0.05$) (Fig. 6.4A, C, E, *Weight Off, 1st Step*). The group of infants who did not show an after-effect tended to have a statistically lower toe trajectory and less hip and knee flexion when the weight was on ($p < 0.01$) (Fig. 6.4B, D, F, *Weight On Steps*). When the weight was removed, the maximum toe trajectory height and maximum hip or knee flexion achieved in the first step was not different from control ($p > 0.05$).

6.3.2 Hip Torques

Figure 6.5 illustrates averaged hip torques during the swing phase from all infants who showed an after-effect (left panel) and those who did not show an after-effect (right panel). Muscle, interaction, and gravitational torques acting about the hip are illustrated. The solid line surrounded by the gray shading represents the mean and standard error of muscle torque, respectively. The hip muscle torques generated during control steps are comparable between the two groups of infants (Figs 6.5A and B). Hip muscle torques were flexor at the beginning of swing, coinciding with knee flexor muscle torques (Fig. 6.6) as the leg moves up and forward to clear the ground. Towards the end of swing, hip muscle torques became very low or switched to the extensor direction (Fig. 6.5A). This corresponds with knee flexor muscle torque during late swing (see Fig. 6.6A and B) and may reflect activity in the hip extensor/knee flexor hamstrings muscle group to slow the leg

Figure 6.4. Change in Kinematic Variables with the Weight On and Off.

Line graphs representing the change in maximum toe trajectory (*A*, *B*), maximum hip flexion (*C*, *D*), and maximum knee flexion (*E*, *F*) under different walking conditions (control, weight on, weight off 1st step). Each point in the plots is the average from all infants in each group with standard errors represented by the error bars. Single asterisks represent significance at $p < 0.05$. Double asterisks represent significance at $p < 0.01$.

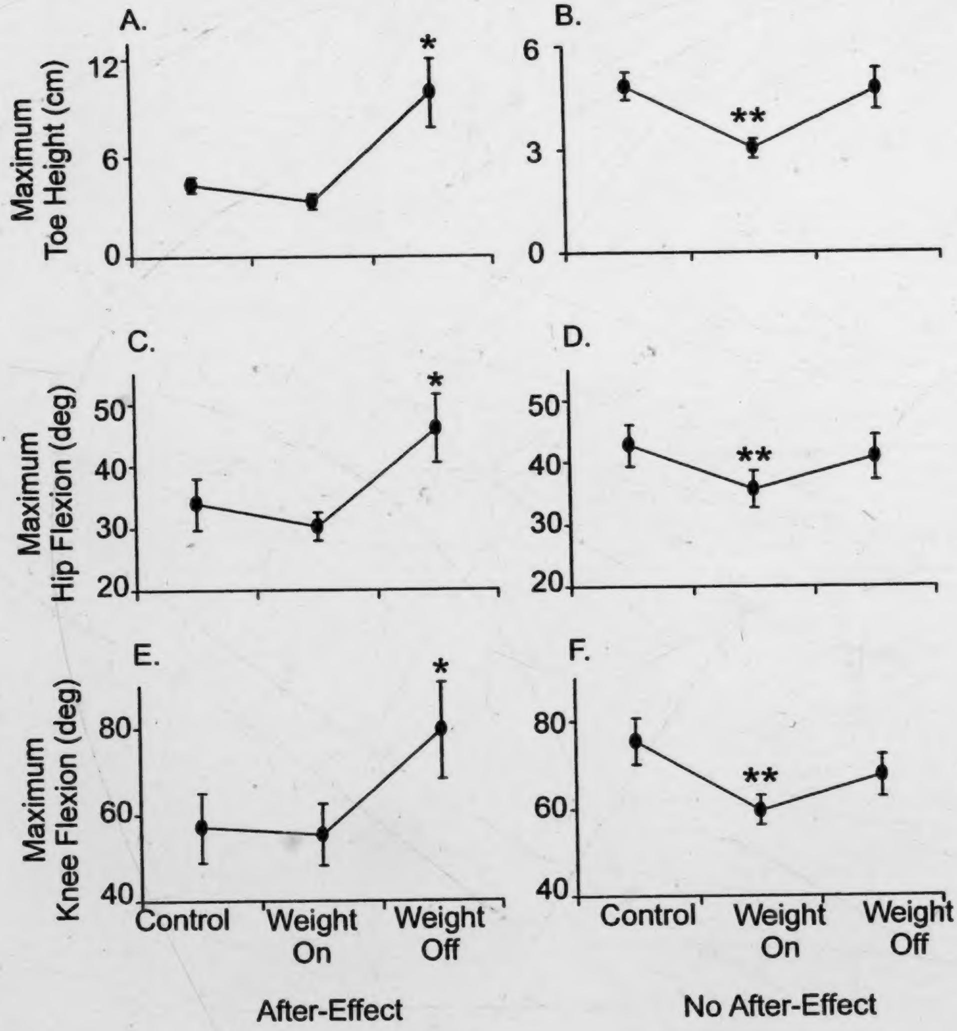
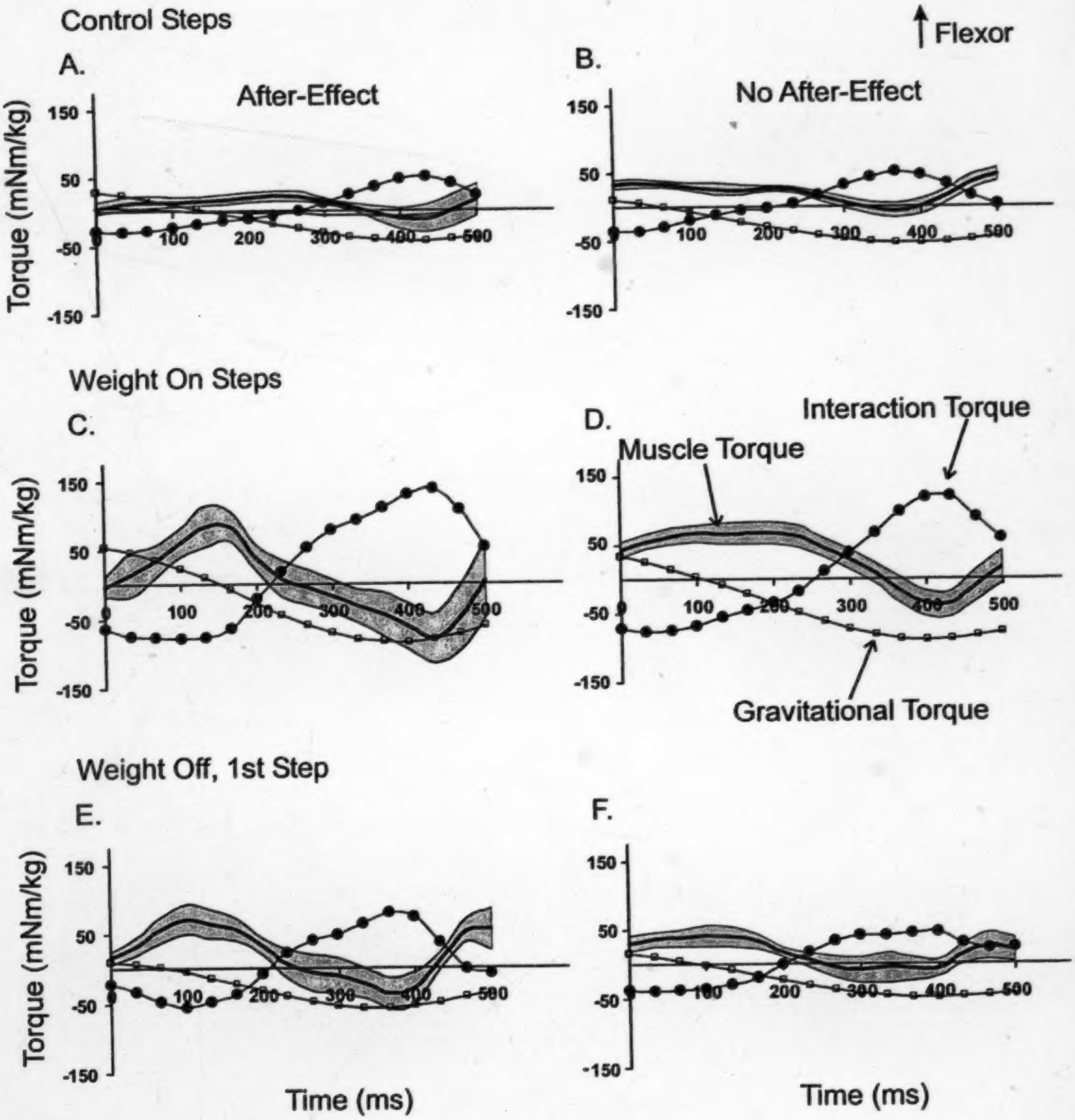

A.
B.
C.
D.
E.
F.
Maximum Toe Height (cm)
Maximum Hip Flexion (deg)
Maximum Knee Flexion (deg)
0
6
12
3
20
30
40
50
60
80
*
**
Control
Weight On
Weight Off
After-Effect
No After-Effect

Figure 6.5. Averaged Hip Torques with the Weight On and Off.

Averaged hip torques for both groups of infants under different walking conditions (control (*A*, *B*), weight on (*C*, *D*), weight off 1st step (*E*, *F*)). Torque values were normalized for body mass and in time. Positive values are flexor and negative values are extensor at the hip. Thick black line surrounded by gray shading represents averaged hip muscle torque and the standard error of hip muscle torque, respectively. Interaction torque, thick black line with filled circles. Gravity torque, open squares with thin black line.


Control Steps
↑ Flexor
A.
After-Effect
B.
No After-Effect
Weight On Steps
C.
D.
Interaction Torque
Muscle Torque
Gravitational Torque
Weight Off, 1st Step
E.
F.
Torque (mNm/kg)
150
50
-50
-150
0
100
200
300
400
500
Time (ms)

down and prepare for the support phase. The effect of gravity is greatest in the latter part of the swing phase and tends to pull the hip toward extension. This appears to be the main torque acting about the hip to help in braking the leg to prepare for foot contact. This would also account for the low muscle torque generated at this point given that the torque due to gravity is sufficient to slow the leg down at the end of swing.

When the weight is on the leg, there is an overall increase in hip muscle torque in both groups of infants (Fig. 6.5C and *D*). The effect of the additional weight on the leg is also reflected in the interaction and gravity torques throughout the swing phase. At the beginning of swing, there was greater gravity torque produced in the flexor direction as the hip is facilitated into flexion by the extra weight. There was also higher hip flexor muscle torque during the first half of swing, compared to control. During the second half of swing phase, greater hip extensor muscle torque was generated, coinciding with the large increase in knee flexor muscle torque (see Fig. 6.5*D* and 6.6*D*). This may reflect greater recruitment of the hamstrings muscles to compensate for the large flexor interaction torque, thus decelerating the limb in preparation for support phase. Towards the end of swing, there is also a larger hip extensor torque due to gravity as a result of the extra weight on the leg, which would also help to decelerate the limb in preparation for support.

There was little qualitative difference between the torques produced in the step after the weight was removed and controls steps in the infants who did not show an after-effect (Fig. 6.5F). In the infants who showed an after-effect, there was greater hip flexor muscle torque at the beginning of the swing phase of the first step with the weight off, compared with control steps. This corresponds with the higher toe trajectory and greater hip flexion in the 1st step after the weight was removed (see Fig. 6.2 and 6.4).

6.3.3 *Knee Torques*

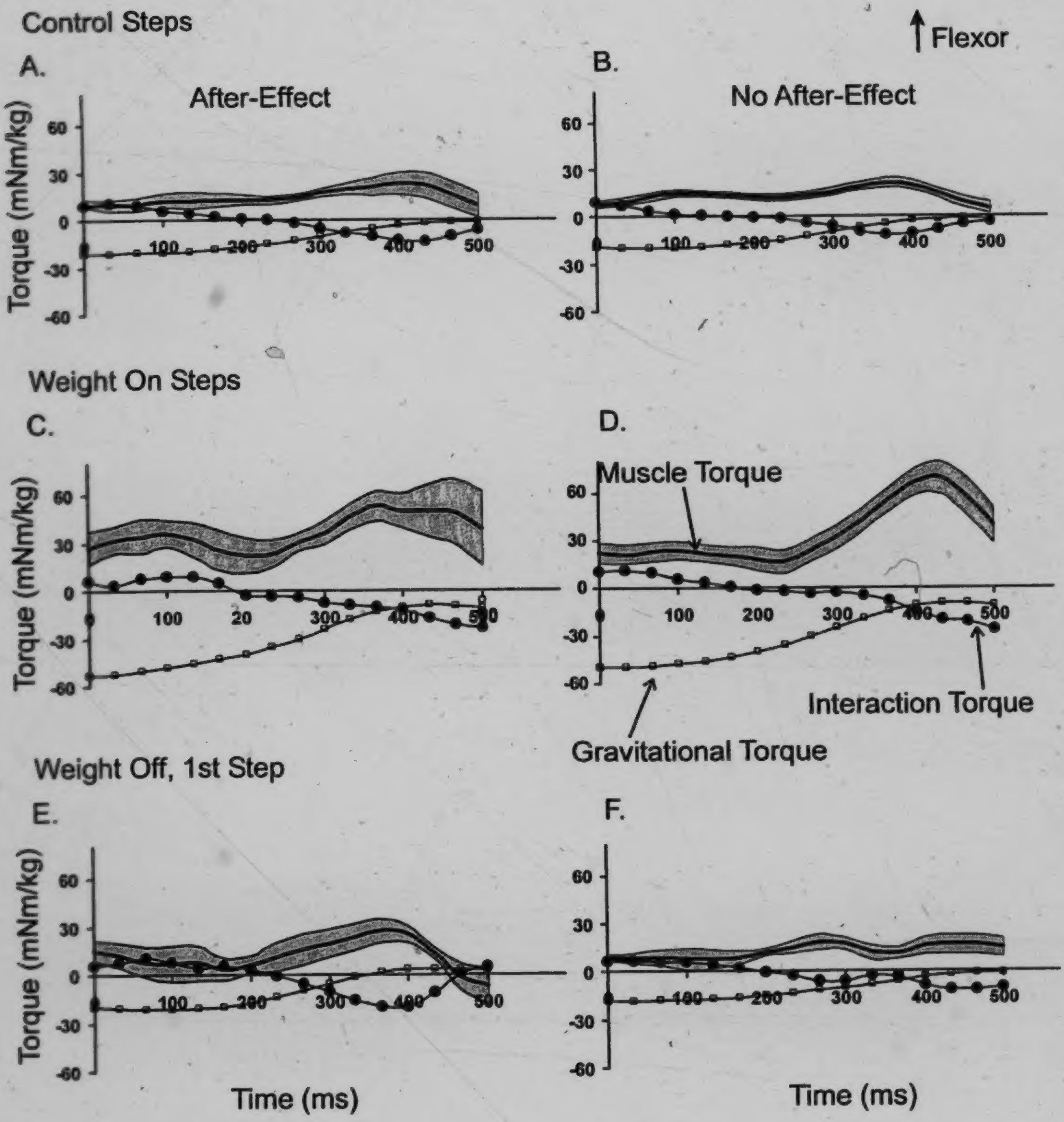
Figure 6.6 illustrates the averaged knee torques during the swing phase from all infants who showed an after-effect (left panel) and those who did not show an after-effect (right panel). Muscle, interaction, and gravitational torques acting about the knee are illustrated as for the hip torque figures. Knee torques generated during control steps are comparable between the two groups of infants (Fig. 6.6*A* and *B*). At the beginning of swing, knee flexor muscle torques are lowest while gravitational torques are extensor and at their largest. This reflects the influence of gravity assisting the forward movement (knee extension) of the leg as flexion is initiated. During the first half of swing, knee flexor muscle torque gradually increases as the leg is lifted up and forward to clear the ground while gravitational torques gradually decrease. Knee flexor muscle torques continue to increase through to late swing as the leg is moved forward through swing to counteract the extensor interaction torques. Knee flexor muscle torques reached highest values towards the end of swing, serving to slow the leg in preparation for foot contact.

When the weight was on the leg, all of the torque components tended to increase in both groups of infants (Fig. 6.6C and *D*). The effect of the extra weight on the leg is reflected in the greater torque due to gravity, especially at the beginning of swing. Knee muscle torques show greater flexor activity, likely to counteract some of the extensor effect of gravity at this point while at the same time helping to clear the ground. Towards the end of swing, gravity torques approach zero while knee muscle torque reaches peak flexor activity.

When the weight was removed, the torque profiles at the knee in the infants who did not show an after-effect returned immediately to normal (Fig. 6.6*F*). In the second

Figure 6.6. Averaged Knee Torques with the Weight On and Off.

Averaged knee torques for both groups of infants under different walking conditions (control (*A*, *B*), weight on (*C*, *D*), weight off 1st step (*E*, *F*)). Torque values normalized for body mass and in time. Positive values are flexor and negative values are extensor at the knee. Thick black line surrounded by gray shading represents averaged knee muscle torque and the standard error of knee muscle torque, respectively. Interaction torque, thick black line with filled circles. Gravity torque, open squares with thin black line.


Control Steps
↑ Flexor
A.
After-Effect
B.
No After-Effect
Weight On Steps
C.
D.
Muscle Torque
Interaction Torque
Gravitational Torque
Weight Off, 1st Step
E.
F.
Torque (mNm/kg)
60
30
0
-30
-60
100
200
300
400
500
Time (ms)

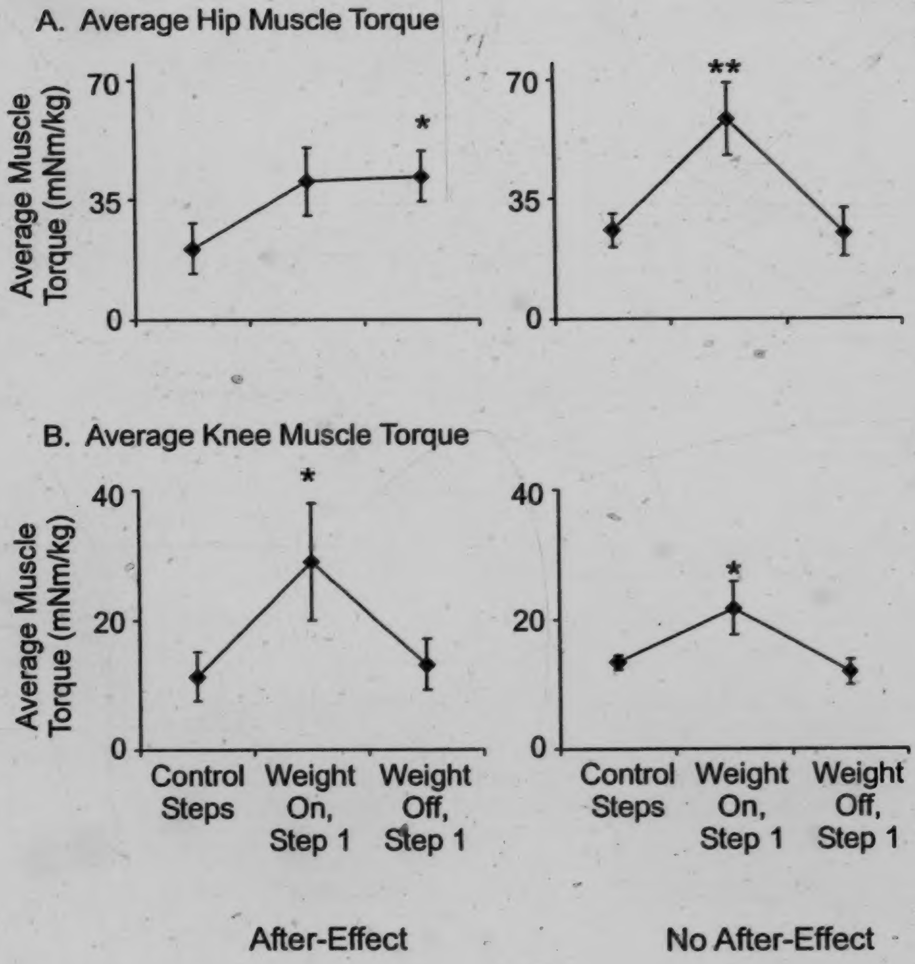
group of infants, the observed after-effect was only slightly reflected in the torque profiles (Fig. 6.6*E*). During the beginning of swing, knee muscle torque in the first step with the weight off did not appear to be greatly different from control steps. Near the end of swing, flexor muscle torque was higher than control, probably to help counteract the extensor interaction torque at the knee at this time.

6.3.4 *Quantification of Muscle Torques*

For each infant, the average muscle torque over the first half of swing phase was calculated. These averaged torque values were then averaged across infants in each group (after-effect and no after-effect group) to quantify the changes in hip and knee muscle torques between the different walking conditions (control, weight on, weight off 1st step) (Fig. 6.7). In the first step taken with the weight on, there was an immediate increase in hip and knee muscle torques during the first half of the swing phase (Fig. 6.7*A* and *B*, *Weight On, 1st Step*). Hip and knee muscle torques remained elevated throughout walking sequences with the weight on (see Fig. 6.5*C* and *D* and 6.6*C* and *D*). Despite the increased hip and knee muscle torques, it appears that the infants, especially those that did not show an after-effect, still had difficulty with maintaining the same level of ground clearance with the weight on since toe trajectory profiles remained slightly lower compared to control steps (see Fig. 6.2). When the weight was removed, hip and knee muscle torques during the beginning of swing returned immediately to normal values in the infants who did not show an after-effect (Fig. 6.7*A* and *B*, right panel, *Weight Off, 1st Step*). In contrast, the group of infants who did show an after-effect continued to produce elevated hip muscle torques, reflecting the existence of an after-effect in these infants ($p < 0.01$, Fig. 6.7*A*, left panel,

Figure 6.7. Quantification of Hip and Knee Muscle Torques.

Line graphs representing averaged hip (*A*) and knee (*B*) muscle torque values during the first half of swing phase. Each point in the plots is the averaged muscle torque from all infants in each group with standard errors represented by the error bars. Single asterisks, $p < 0.05$. Double asterisks, $p < 0.01$.


A. Average Hip Muscle Torque
Average Muscle Torque (mNm/kg)
70
35
0
*
**
B. Average Knee Muscle Torque
Average Muscle Torque (mNm/kg)
40
20
0
*
*
Control Steps
Weight On, Step 1
Weight Off, Step 1
Control Steps
Weight On, Step 1
Weight Off, Step 1
After-Effect
No After-Effect

Weight Off, 1st Step). Knee muscle torques during the beginning of swing in the first step with the weight off were not significantly different from control (Fig. 6.7B, right panel, *Weight Off, 1st Step*).

6.4 Discussion

The main finding was that all infants responded to the extra weight on the leg and did so by recruiting greater flexor muscle torque at the knee and hip. This was exemplified by the increase in hip and knee flexor muscle torque, which occurred within the first step with the weight on (Fig. 6.5, 6.6, and 6.7). Of further interest was whether infants showed an after-effect after the weight was removed, which would indicate that learning had occurred. The criteria we used (see Methods) resulted in a separation of the infants into 2 groups – those who showed a high stepping response after removal of the weight (n = 7), and those who did not (n = 15). However, the scatterplot in figure 6.1 demonstrates a continuum of responses after removal of the weight, rather than a clear separation of infants into 2 groups.

A limitation in the criteria we used to assess the presence of an after-effect was the fact that infant stepping is variable and thus differences in the kinematic variables after removal of the weight could be difficult to identify. Another possibility is that the apparent 'after-effects' we observed were not actually indicative of any learning. The change in sensory input with removal of the sandbag weight could have contributed to the appearance of a high step. This possibility cannot be definitively ruled out by the present results. The fact that high stepping was primarily observed in only the first step after removal of the weight supports the possibility that the change in sensory input is responsible for the apparent after-effect. In addition, if long-term adaptive strategies were involved, one would predict that there would be a gradual improvement in limb trajectory over time with the weight on. Generally, however, any time-dependent pattern of adaptation could not be discerned by a step-by-step analysis of the change in kinematic parameters (Fig. 6.2A). Thus, the separation of the infants into 2 groups may turn out to be an arbitrary decision.

Whether the amount of weight experienced by an infant influenced the adaptation is unclear. The average additional weight experienced by the infants was 76% of the total weight of the limb. It is possible that this was too heavy and prevented proper adaptation of the stepping pattern to the extra weight. Indeed, most infants showed difficulty with stepping with the weight on, shown by the observation that the amount of hip and knee flexion generated when the weight was on was significantly lower than control in most of the infants (Fig. 6.4, right panel). Addressing this issue would require specific testing of the effect of different weights in the same infant by recording repeated trials.

All infants showed an ability to adapt to the stepping pattern to the extra weight on the leg. This was characterized by an increase in hip and knee flexor muscle torque within the first 3 steps taken with the weight on. The rapid and appropriate response to the extra weight suggests a mechanism that could be mediated by reflex pathways. Candidate pathways could include those characterized in reduced cat preparations. Stimulation of hip flexor group I muscle afferents during the swing phase prolongs flexor burst duration and increases flexor burst magnitude in the fictive (Perreault et al. 1995; McCrea et al. 2000; Quevedo et al. 2000) and decerebrate walking cats (Lam and Pearson 2001b). Furthermore, these pathways may have a functional role in mediating flexor activity in response to proprioceptive feedback during the swing phase (Lam and Pearson 2001a).

Whether similar flexor muscle afferent pathways to flexor motoneurons also exist in humans remains to be determined. If they do exist in humans, it is possible that increases in the production of hip and knee flexor activity in response to the extra weight on the leg were mediated via these reflex pathways. In addition, we cannot rule out the possibility that the intrinsic properties of muscles played a role in mediating the increase in muscle torque when the weight was on. Indeed, the angular velocities of the lower limb joints tended to be lower with the added weight compared to control stepping (data not shown) and thus the muscles could have generated more force. Indeed, muscles are able to generate more force as the velocity of contraction is slowed and do so to compensate for inertial loads (Partridge 1966).

Motor learning of discrete tasks is often discussed within the context of an 'inverse internal model', which is defined as an internal representation of the system and as such has the ability to issue a set of motor commands given a desired sensory outcome or movement trajectory (Kawato 1999). As a theory, it provides a compelling framework within which motor learning can be investigated. One prediction of the internal model concept for motor control is that any recalibration of the motor command for a given task in response to a change to the mechanics of the body will be revealed upon unexpected removal of the mechanical disturbance. The recalibration allowed for the resumption of normal trajectories and the reduction in end-point errors in the presence of the perturbing input. Unexpected removal of the disturbance reveals this recalibration in the form of a temporary distortion in movement. Whether adaptive strategies during locomotor tasks employ an inverse internal model is not clear. However, there is some evidence supporting this concept. For example, decerebrate walking ferrets adapted to repeated presentation of an obstacle in the path of the forelimb's trajectory by increasing the height of the paw trajectory. When the obstacle was removed, there was a persistence of the conditioned behaviour for several steps before returning to control levels (Lou and Bloedel 1988). Similarly, in humans there are some reports of after-effects occurring in locomotor tasks after a period of adaptation to a novel environment (Anstis 1995; Gordon et al. 1995; Jensen et al. 1998; Weber et al. 1998). For example, Weber et al. (1998) showed that there is a reconfiguration of the sensorimotor mechanisms that guide the trajectory (direction) of locomotion. Subjects who stepped on a circular treadmill for as little as 7.5 minutes continued to produce a curved trajectory of walking when they were subsequently asked to step blindfolded over ground in a straight line (Weber et al. 1998). Thus, there are some indications that feedforward control, that may or may not involve recalibration of a hypothetical inverse internal model for walking, is available to adapt locomotor output to sustained changes in sensory input. Whether human infants also use feedforward control during adaptations of their stepping pattern could not be determined with certainty using the present paradigm. However, recent unpublished results from this laboratory using a different paradigm (Pang and Yang, unpublished observations) suggest that some infants did have an anticipatory response during obstructed treadmill stepping, thus lending support for the idea that there is some capability for feedforward control during human infant stepping.

Our results are the first to show that human infants can adjust their stepping pattern in response to sustained changes to the mechanics of the leg. Variability inherent in the infants' stepping pattern may have limited our ability to draw definitive conclusions about whether any long-term adaptive strategies were developed in response to stepping with the additional load on the leg. If there were after-effects in some infants, this indicates the possibility that there was a recalibration of the motor commands used to generate stepping. Furthermore, we show that all infants could compensate to the extra load on their leg and did so by recruiting greater flexor torque at the hip and knee joints. This is well before the development of mature and independent walking and suggests that some of these adaptive mechanisms may reside in sub-cortical structures.

6.5 References

Anstis S. Aftereffects from jogging. *Experimental Brain Research* 103:476-478, 1995.

Carrier L, Brustein E, Rossignol S. Locomotion of the hindlimbs after neurectomy of ankle flexors in intact and spinal cats: model for the study of locomotor plasticity. *Journal of Neurophysiology* 77: 1979-1993, 1997.

Gordon CR, Fletcher WA, Jones GM, Block EW. Adaptive plasticity in the control of locomotor trajectory. *Experimental Brain Research* 102: 540-545, 1995.

Gritsenko V, Mushahwar V, Prochazka A. Adaptive changes in locomotor control after partial denervation of triceps surae muscles in the cat. *Journal of Physiology* 533: 299-311, 2000.

Hoy MG, Zernicke RF. The role of intersegmental dynamics during rapid limb oscillations. *Journal of Biomechanics* 19: 867-877, 1986.

Jensen L, Prokop T, Dietz V. Adaptational effects during human split-belt walking: influence of afferent input. *Experimental Brain Research* 119: 126-130, 1998.

Kawato M. Internal models for motor control and trajectory planning. *Current Opinion in Neurobiology* 9: 728-727, 1999.

Lam T, Pearson KG. Proprioceptive modulation of hip flexor activity during the swing phase of locomotion in decerebrate cats. *Journal of Neurophysiology* 86: 1321-1332, 2001a.

Lam T, Pearson KG. The effects of stimulating sartorius muscle afferents during the swing phase of walking in decerebrate cats. *Society for Neuroscience Abstracts* 27: 1060, 2001b.

Lou J-S, Bloedel JR. A new conditioning paradigm: conditioned limb movements in locomoting decerebrate ferrets. *Neuroscience Letters* 84: 185-190, 1988.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233, 2000.

Pang MYC, Yang JF. The initiation of the swing phase in human infant stepping: importance of hip position and leg loading. *Journal of Physiology* 528: 389-404, 2000.

Pang MYC, Yang JF. Inter-limb coordination in human infant stepping. *Journal of Physiology* 533: 617-625, 2001.

Partridge LD. Signal-handling characteristics of load-moving skeletal muscle. *American Journal of Physiology* 210: 1178-1191, 1966.

Pearson KG. Neural adaptation in the generation of rhythmic behavior. *Annual Reviews in Physiology* 62: 723-753, 2000.

Pearson KG, Fouad K, Misiaszek JE. Adaptive changes in motor activity associated with functional recovery following muscle denervation in walking cats. *Journal of Neurophysiology* 82: 370-381, 1999.

Pearson KG, Misiaszek JE. Use-dependent gain change in the reflex contribution to extensor activity in walking cats. *Brain Research* 883: 131-134, 2000.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Schneider K, Zernicke RF, Ulrich BD, Jensen JL, Thelen E. Understanding movement control in infants through the analysis of limb intersegmental dynamics. *Journal of Motor Behavior* 22: 493-520, 1990.

Weber KD, Fletcher WA, Gordon CR, Jones MG, Block EW. Motor learning in the "podokinetic" system and its role during spatial orientation during locomotion. *Experimental Brain Research* 120: 377-385, 1998.

Whelan PJ, Pearson KG. Plasticity in reflex pathways controlling stepping in the cat. *Journal of Neurophysiology* 78: 1643-1650, 1997.

Winter DA. *The biomechanics and motor control of human gait: normal, elderly and pathological.* Waterloo, ON: University of Waterloo Press, 1991.

Yang JF, Lam T. Adaptation to loading of the limb during the swing phase in human infant stepping. *Society for Neuroscience Abstracts* 27: 1075, 2001.

Yang JF, Stephens MJ, Vishram R. Infant stepping: a method to study the sensory control of human walking. *Journal of Physiology* 507: 927-937, 1998a.

Yang JF, Stephens MJ, Vishram R. Transient disturbances to one limb produce coordinated, bilateral responses during infant stepping. *Journal of Neurophysiology* 79: 2329-2337, 1998b.

CHAPTER 7

GENERAL DISCUSSION

7.1 Summary

One of the most remarkable aspects of the nervous system is its capability for plasticity. The intricate control of locomotion by the nervous system is no less remarkable in its adaptive qualities. The capability for adaptation is underscored even more by the necessity imposed on animals in natural settings where continuous adjustments to the walking pattern are required while traversing over constantly changing and unpredictable terrain. Not only can the locomotor pattern be adapted to generate different forms of locomotion (e.g. different directions, slope walking, crouched walking), it can also be adapted to respond to perturbations during the course of movement or changes to limb properties during development or after injury. The projects presented in this thesis have addressed each of these features of the neural control of locomotion. First, can the output of the locomotor pattern generator be transformed into different forms of human stepping? In Chapter 2, the ability of the locomotor system to generate different directions of stepping was shown to be present even before the onset of independent walking in humans. The data were consistent with and further contributed to the idea that central locomotor networks can be adapted to generate different locomotor tasks. The second feature of locomotor adaptation addressed in this thesis is the major role that afferent feedback plays in shaping the output of the locomotor pattern. In Chapter 3, it was shown that changes in proprioceptive feedback strongly modulate hip flexor activity during the swing phase of decerebrate cat locomotion. Input from large muscle afferents is likely a major contributor to this modulation (Chapter 4). These results led to the final projects, which were based on the concept that proprioceptive feedback during walking provides information not only for transient changes during locomotion, but also to more sustained changes to the properties of the body (Chapters 5 and 6). Lasting perturbations of the limb during the swing phase of locomotion triggered adaptive modifications to swing phase activity. These adaptive modifications may have involved lasting changes to the locomotor generating system. Thus, adaptation in the locomotor system can be immediate or involve longer-term mechanisms (learning). Immediate adaptations can occur according to performance requirements (e.g. changing walking direction) or sensory disturbances (e.g. loading of the limb). Longer-term adaptive modifications (learning) occur in response to training or lasting changes to the properties of the body.

7.2 Future Directions

7.2.1 Neural Control of Different Forms of Locomotion

The study presented in Chapter 2 was the first to show data consistent with the idea that all different directions of human walking are controlled by a common locomotor generator. Data were collected from human infants, which further suggest that the ability to switch between different directions of stepping is mediated by neural centres located in brainstem or spinal cord structures. The concept that the control of different motor behaviours may be shared among neural networks is a strong argument for the adaptability of the locomotor system. An examination of the responses to sensory input during different forms of walking yields further insight into the adaptability of the locomotor system. The response to speed was already examined in the present thesis and found to be similar regardless of the direction of walking (Chapter 2). The response to other types of sensory input is more specific to the direction of walking. Recent studies comparing forward stepping with either sideways (Pang and Yang, in press) or with backward walking (Buford and Smith 1993; Duysens et al. 1996) have shown how sensory input is selectively gated depending on the direction of locomotion. Pang and Yang (in press) have shown that during infant stepping, the most effective input that initiates the swing phase depends on the direction of walking. Hip extension during late-stance is strongly effective in initiating the swing phase during forward walking while hip abduction or adduction is more effective during sideways walking. Phase-dependent responses to cutaneous stimulation are also tailored to the direction of walking in cats (Buford and Smith 1993) and in adult humans (Duysens et al. 1996). If one accepts the concept of a common locomotor control system for different directions of walking, the locomotor central pattern generator can be envisaged as a system that receives convergence from a variety of sensory inputs and that possesses flexibility vis-à-vis its ability to tailor its output depending on the type of sensory input and the direction of walking. There is already some indication that this flexibility and adaptability is present in the human locomotor system even before the onset of independent walking (Lamb and Yang 2000; Pang and Yang, in press).

Another issue would be whether or not learning in one direction of stepping transfers to all directions of stepping. Such generalization of motor learning has been shown for visuomotor tasks and upper limb movements (reviewed in Kawato 1999) as well as for the control of perceived direction of walking in adult humans (Earhart et al. 2001, 2002). In human infants, demonstrating that adaptation of the locomotor pattern during forward stepping transfers to other directions of stepping, in response to the same chronic disturbance, would provide further evidence for the idea that the locomotor system mediating different directions of stepping is shared. For example, if infants practiced forward stepping with the additional weight on, would any after-effects upon removal of the weight be elicited during backward or sideways stepping? If adaptive responses to the extra weight on the leg were mediated through a shared circuitry that included control of different directions of stepping, then one might expect that after-effects would be observed even after a change in stepping direction and removal of the weight.

Differences between adult and infant stepping in the motor patterns for forward and backward walking were also discussed in Chapter 2 (Lamb and Yang 2000). The common feature across studies that compared adult forward and backward walking is the variability in muscle activation patterns while the kinematic patterns of the limbs are preserved (the movement trajectory of backward walking being a reversal of forward walking) (Thorstensson 1986; Winter et al. 1989; Grasso et al. 1998). The reverse was observed in human infants – muscle activation patterns generally tended to be similar while no preservation of movement trajectory was seen. Based on these observations, we proposed that the control of kinematic variables could be originating from higher brain centres (Lamb and Yang 2000). Examination of the locomotor pattern during forward and backward walking from human subjects aged 9 months to early childhood years (or even older) may yield some insight into the timeline for the development of this control. Is the transfer from the control of muscle activation pattern to mainly controlling kinematic variables during stepping correlated with certain milestones during childhood development, such as the onset of independent walking or the development of more advanced locomotor tasks such as skipping?

7.2.2 Proprioceptive Regulation of Flexor Activity during the Swing Phase of Walking

Much of the focus of past investigations on the proprioceptive regulation of locomotion has been that during the stance-to-swing phase transition or the stance phase. In Chapters 3 and 4, the focus was on the proprioceptive regulation of flexor activity during the swing phase of decerebrate cat locomotion. Previous reports from fictive decerebrate preparations have identified several pathways by which flexor muscle afferents influence the output of flexor motoneurons during locomotion (Perreault et al. 1995; Degtyarenko et al. 1998; McCrea et al. 2000; Quevedo et al. 2000). The results from the projects in this thesis extend those of Hiebert et al. (1996) and indicate that the flexor muscle afferent pathways identified in fictive preparations could have a functional role in mediating flexor muscle activity during the swing phase of walking in cats. In the present thesis, the focus was on the effect of hip flexor muscle afferents on hip flexor muscle activity. However, excitatory effects from group I knee and ankle flexor muscle afferents to their homologous motoneurons have also been shown in fictive preparations (Quevedo et al. 2000) and are indicated in walking preparations (Hiebert et al. 1996). Whether these pathways play a functional role during treadmill locomotion should be further investigated. This information would help to complete our understanding of known effects of flexor muscle afferents to flexor muscle activity during walking and could be of use in subsequent investigations of the adaptive capabilities of the locomotor system (see section 7.2.3).

The study presented in Chapter 3 focused on hip flexor activity and demonstrated a particularly potent influence from the sartorius muscle during the swing phase of treadmill locomotion. Elimination of input from the sartorius muscle, by denervating it, resulted in a marked decrease in the response to resisting limb flexion (Chapter 3). Electrical stimulation of the sartorius nerve indicated that input from group I sartorius muscle afferents is likely involved in this response (Chapter 4). Mechanical activation of the muscle receptors by applying stretches to the sartorius muscle during walking will provide functionally relevant evidence for the role of group I muscle afferents. This may prove to be difficult, however, since the sartorius muscle is thin, broad, and does not have a well-defined tendinous insertion and thus would be difficult to be securely affixed to a mechanical device. If a method could be devised, it would also be interesting to investigate whether there are separate effects from the two compartments of the sartorius muscle (the anterior and the medial head). This could be done by transecting the nerve branch to one of the compartments thereby leaving only one of the heads functional and able to respond to stretch.

The effects from group II flexor muscle afferents on flexor activity during decerebrate locomotion was also examined in Chapter 4. These effects are variable in fictive and treadmill locomotor preparations (Perreault et al. 1995; Hiebert et al. 1996; McCrea et al. 2000). We also found that the effect of group II sartorius muscle afferents on hip flexor activity during treadmill locomotion was variable but often showed a time-dependent transition from an inhibitory to an excitatory effect (Chapter 4). Could this be due to a diminishment of group II inhibitory effect, revealing an excitatory group I effect? This could be investigated by targeted inhibition of group I muscle afferent effects on motoneuron excitability. Strategies using ischemia could be applied to selectively block transmission in group I muscle afferents (Grey et al. 2001). Separation of group I from group II effects could also be achieved by applying continuous activation of primary spindle endings by constant vibration of the muscle. Electrical stimulation at group II strengths, applied against this background of continuous muscle vibration, would tend to selectively activate secondary afferents and presumably not recruit more group I muscle afferents (which are already maximally activated by the vibration) (Baldissera et al. 1981). Of course, this method would be contingent on devising a secure method to apply mechanical perturbations to the muscle of interest. If the time-dependent transition from an inhibitory to an excitatory effect is due to the emergence of group I effects, then excitatory effects should not be reproduced when these strategies are employed.

7.2.3 Learning during Walking Tasks

An important application of the knowledge obtained about proprioceptive input during locomotor activity is how this input mediates long-term adaptive changes to the locomotor pattern after sustained changes to the biomechanical or neuromuscular properties of the body. An example of how this concept is applied was demonstrated by Whelan and Pearson (1997) who reported changes in the gain of reflexes from the medial gastrocnemius muscle after transection of the nerves to its synergists. In this case, knowledge of the relative strengths of reflex pathways from various ankle extensor muscle afferents led to the ability to identify this specific change in reflex modulation associated with the adaptive modifications after nerve transection. Adaptive modifications clearly occur in response to chronic loading of the limb during the swing phase (Chapters 5 and 6) and in response to weakening of knee flexor activity (Chapter 5). Are these adaptive modifications also associated with changes in reflex pathways from flexor muscle afferents to flexor motoneurons? More generally, at what level of the nervous system are the plastic changes associated with the adaptive responses located? The observations of Carrier et al.

(1997) suggest that plasticity (in response to ankle flexor neurectomy) can occur at both supraspinal and spinal levels. Is this the case for adaptive responses to the additional weight on the limb (Chapter 5)? This could be addressed by first training cats to walk on a treadmill with the weight on. After adaptation, an acute experiment could be performed where the animal would first be decerebrated and then spinalized. The first question to be addressed would be whether any adaptive changes (such as increases in flexor muscle activity) were persistent after decerebration and spinalization. If so, it would suggest that adaptive mechanisms resided in brainstem, cerebellar, or spinal structures. Secondly, the response to removal of the weight could be observed, either before or after spinalization. This should be the first time that the weight has been removed and if there were an after-effect, it would suggest that learning had taken place and that areas rostral to the brainstem are capable of mediating this long-term adaptation in response to extra weight on the limb. These experiments would only provide information about the site of plasticity, and not the nature of the mechanisms whereby learning was enabled. Furthermore, they are limited by the inevitability that locomotor ability may be so affected by the decerebration and/or spinalization that failure to observe persistent adaptive effects with the weight on or after-effects after removal of the weight may not reflect the option that adaptive changes resided in brainstem, cerebellar, or spinal structures.

One method to approach the nature of the mechanisms used to adapt to the additional weight would be to investigate changes in reflex pathways. One possible outcome is that changes in the gain of reflex pathways (analogous to the report of Whelan and Pearson (1997)) were involved. The projects in this thesis have showed that in treadmill walking cat preparations, sartorius muscle afferents have an excitatory effect on hip flexor activity (Chapters 3 and 4). However, the degree of contribution from other flexor muscle afferents has not been investigated. Examination of the possibility of changes in the gain of reflex pathways would first require more information about the reflex effects from flexor muscle afferents on flexor muscle activity during the swing phase (see above, section 7.3.2). A comparison of the relative effects of these reflex pathways between trained and untrained animals might show some differences and yield insight into whether changes in transmission in reflex pathways are involved in mediating adaptive responses to the extra weight. A limitation to this method is that the locomotor rhythm is strongly entrained by the speed of the treadmill and effects on flexor burst or cycle duration may be masked (see Chapters 3 and 4). However, effects on the amplitude of reflex responses to stimulation of flexor muscle afferents may at least provide information about changes to the output of motoneurons during locomotion (for example, via monosynaptic reflex pathways).

In both the human infant and cat studies, evidence for learning was given by the fact that after-effects were observed after removal of the extra weight. Learning of new tasks is often discussed in a framework of an 'inverse internal model' of the dynamics of the limb (Kawato 1999). This concept predicts that control of movement trajectory is controlled by adjusting the motor output (i.e. muscle activation and torque generation). Furthermore, a prediction of the sensory consequences of the movement is also available to the system via the internal model. Given this framework, one might expect that as conditions change, the motor program does not compensate for the changes until experience within the new condition has been obtained. Thus, depending on the extent of the perturbation, initial movements performed within the new condition should produce errors in terms of a mismatch between the expected kinematic pattern of the movement and the motor command that was issued. With experience, however, this mismatch should be corrected as the motor commands are adjusted to meet the new demands of the system or environment. Behaviourally, one would expect this adjustment period to be manifested as a gradual, experience-dependent pattern of adaptation. In the studies presented in Chapters 5 and 6, however, there was not always this gradual pattern of adaptation in compensation for the extra weight, particularly in the infants. An apparent lack of a time-dependent pattern of adaptation could have been due to the inherent variability in infant stepping. Variability was also present between the cats studied. When additional weight was added to the hindlimb of intact cats, one of the animals showed an immediate response to the weight (high stepping) while more gradual adjustments in limb trajectory were observed in the other cats. Notwithstanding factors due to variability and individual differences between animals, proprioceptive feedback pathways, which sense changes in length and load input, may have been involved in the immediate responses to additional weight on the limbs of cats and infants and thus partly account for the lack of an observable experience-dependent pattern of adaptation. As shown in Chapters 3 and 4, flexor activity during the swing phase is strongly modulated by proprioceptive feedback pathways. If such pathways were involved in the adaptation to the loading of the limb, then any gradual, experience-dependent adaptive pattern to the additional weight would be masked. Thus, it would be important to separate the effects of any immediate proprioceptive feedback responses from the effects due to the longer-term adaptation process. This was partly addressed in the experiment presented in Chapter 5 whereby the nerve to the semitendinosus muscle was cut, thereby severely compromising afferent input from this major knee flexor muscle. In this situation, a time-dependent pattern of adaptation was observed as a gradual increase in the slope of the initial toe trajectory and a short-lived after-effect was observed when the weight was removed. Another approach would be to remove the weight sooner, before long-term adaptive changes presumably occur. For example, in the cat that showed an immediate high stepping as soon as the weight was added, a determination of whether or not this immediate high stepping was an immediate proprioceptive feedback response could be achieved by removing the weight sooner, perhaps after only 1 full day with the weight on, and noting the presence or absence of after-effects. The lack of an after-effect in this case would support the notion that the early adaptive response was mediated by reflex pathways and indicate that learning had not yet taken place.

Another issue that could be examined in these learning paradigms is the extent to which learning in one specific locomotor task transfer to other locomotor tasks. This could be addressed in a similar manner as that described for the different directions of infant stepping (section 7.2.1). In cats, this could readily be investigated by first training cats to walk on a treadmill or along a level, unobstructed walkway and allow them to adapt to an extra load strapped around their leg. Would these trained cats then be able to perform other locomotor tasks, such as obstacle avoidance or walking along a pegged walkway, without having to undergo another learning period?

Finally, an understanding of adaptive strategies used to respond to additional loading of the limb should not be limited only to activity during the swing phase of walking. Indeed, previous investigations that have examined adaptive strategies for stepping over obstacles compared with level walking have noted postural adjustments made in preparation for clearance of the obstacle (Lavoie et al. 1995; McFadyen et al. 1999). Some indications for postural adjustments before paw lift-off were noted in Chapter 5. A more detailed examination of both flexor and extensor muscle activity from both hindlimbs would be valuable to characterize the full adaptive strategy in response to perturbations during skilled locomotion.

7.3 References

Baldissera F, Hultborn H, Illert M. Integration in spinal neuronal systems. In: *Handbook of Physiology. Section 1: The Nervous System, Volume II. Motor Control, Part 2,* edited by JM Brookhart and VB Mountcastle. Bethesda, MD: American Physiological Society, 1981, pp. 2509-2595.

Buford JA, Smith JL. Adaptive control for backward quadrupedal walking. III. Stumbling corrective reactions and cutaneous reflex sensitivity. *Journal of Neurophysiology* 70: 1102-1114, 1993.

Carrier L, Brustein E, Rossignol S. Locomotion of the hindlimbs after neurectomy of ankle flexors in intact and spinal cats: model for the study of locomotor plasticity. *Journal of Neurophysiology* 77: 1979-1993, 1997.

Degtyarenko AM, Simon ES, Norden-Krichmar T, Burke RE. Modulation of oligosynaptic cutaneous and muscle afferent reflex pathways during fictive locomotion and scratching in the cat. *Journal of Neurophysiology* 79: 447-463, 1998.

Duysens J, Tax AAM, Murrer L, Dietz V. Backward and forward walking use different patterns of phase-dependent modulation of cutaneous reflexes in humans. *Journal of Neurophysiology* 76: 301-310, 1996.

Earhart GM, Jones GM, Horak FB, Block EW, Weber KD, Fletcher WA. Forward versus backward walking: transfer of podokinetic adaptation. *Journal of Neurophysiology* 86: 1666-1670, 2001.

Earhart GM, Jones GM, Horak FB, Block EW, Weber KD, Fletcher WA. Transfer of podokinetic adaptation from stepping to hopping. *Journal of Neurophysiology* 87: 1142-1144, 2002.

Grasso R, Bianchi L, Lacquaniti F. Motor patterns for human gait: backward versus forward locomotion. *Journal of Neurophysiology* 80: 1868-1885, 1998.

Grey MJ, Ladouceur M, Andersen JB, Nielsen JB, Sinkjaer T. Group II muscle afferents probably contribute to the medium latency soleus stretch reflex during walking in humans. *Journal of Physiology* 534: 925-933, 2001.

Hiebert GW, Whelan PJ, Prochazka A, Pearson KG. Contribution of hind limb flexor muscle afferents to the timing of phase transitions in the cat step cycle. *Journal of Neurophysiology* 75: 1126-1137, 1996.

Kawato M. Internal models for motor control and trajectory planning. *Current Opinion in Neurobiology* 9: 728-727, 1999.

Lamb T, Yang JF. Could different directions of infant stepping be controlled by the same locomotor central pattern generator? *Journal of Neurophysiology* 83: 2814-2824, 2000.

Lavoie S, McFadyen B, Drew T. A kinematic and kinetic analysis of locomotion during voluntary gait modification in the cat. *Experimental Brain Research* 106: 39-56, 1995.

McCrea DA, Stecina K, Quevedo J, Gosgnach S. Flexor group II muscle afferents can enhance flexor activity during fictive locomotion. *Society for Neuroscience Abstracts* 26: 1233, 2000.

McFadyen BJ, Lavoie S, Drew T. Kinetic and energetic patterns for hindlimb obstacle avoidance during cat locomotion. *Experimental Brain Research* 125: 502-510, 1995.

Perreault M-C, Angel MJ, Guertin P, McCrea DA. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *Journal of Physiology* 487: 211-220, 1995.

Quevedo J, Fedirchuk B, Gosgnach S, McCrea DA. Group I disynaptic excitation of cat hindlimb flexor and bifunctional motoneurones during fictive locomotion. *Journal of Physiology* 525: 549-564, 2000.

Thorstensson A. How is the normal locomotor pattern modified to produce backward walking? *Experimental Brain Research* 61: 664-668, 1986.

Whelan PJ, Pearson KG. Plasticity in reflex pathways controlling stepping in the cat. *Journal of Neurophysiology* 78: 1643-1650, 1997.

Winter DA, Pluck N, Yang JF. Backward walking: a simple reversal of forward walking? *Journal of Motor Behavior* 21: 291-305, 1989.

APPENDIX 1

EQUATIONS OF MOTION FOR THE ESTIMATION OF JOINT TORQUES DURING THE SWING PHASE OF LOCOMOTION

These formulas were used to estimate torques at the hip, knee, and ankle during the swing phase of infant stepping. The same equations were used for the analysis of swing phase during cat locomotion except that calculations of the mass, lengths, and moments of inertia of the segments were based on data from Hoy and Zernicke (1985). Data from Schneider et al. (1990) and Winter (1990) provided the basis for these estimations in the human infants. Measurement units are indicated in the parentheses.

L (segment length)
m (body mass)

Subscripts:
3 = thigh segment
2 = shank segment
1 = foot segment

Human Infants:
Moment Arms (m)
$r_3 = L_3 \cdot 0.4859$
$r_2 = L_2 \cdot 0.4377$
$r_1 = L_1 \cdot 0.3469$

Segment Masses (kg)
$m_3 = 0.0661 \cdot m$
$m_2 = 0.0334 \cdot m$
$m_1 = 0.0097 \cdot m$

Moments of Inertia
$I_3 = m_3 \cdot (0.323 \cdot L_3)^2$
$I_2 = m_2 \cdot (0.302 \cdot L_2)^2$
$I_1 = m_1 \cdot (0.475 \cdot L_1)^2$

Cats:
Moment Arms (m)
$r_3 = L_3 \cdot 0.443$
$r_2 = L_2 \cdot 0.423$
$r_1 = L_1 \cdot 0.4861$

Segment Masses (kg)
$m_3 = 0.0502 \cdot m$
$m_2 = 0.0241 \cdot m$
$m_1 = 0.0101 \cdot m$

Moments of Inertia
$I_3 = m_3 \cdot (0.443 \cdot L_3)^2$
$I_2 = m_2 \cdot (0.423 \cdot L_2)^2$
$I_1 = m_1 \cdot (0.4861 \cdot L_1)^2$

$\theta_3, \dot{\theta}_3, \ddot{\theta}_3$ *(thigh segment angle, velocity, and acceleration)*
$\theta_2, \dot{\theta}_2, \ddot{\theta}_2$ *(shank segment angle, velocity, and acceleration)*
$\theta_1, \dot{\theta}_1, \ddot{\theta}_1$ *(foot segment angle, velocity, and acceleration)*

$\ddot{x}_3$ (hip linear acceleration in the x-direction)
$\ddot{y}_3$ (hip linear acceleration in the y-direction)

if the weight was on:
p = distance from knee to centre of weight
wt = mass of additional weight
$m_2 = m_2 + wt$
$I_2 = I_2 + wt \cdot (L2 \cdot p)^2$

Constants:
$\beta_1 = (m_1 \cdot L_3) \cdot r_1$
$\beta_2 = (m_1 \cdot L_2) \cdot r_1$
$\beta_3 = m_1 \cdot r_1$
$\beta_4 = m_1 \cdot L_2 \cdot L_3$
$\beta_5 = (m_2 \cdot L_3) \cdot r_2$
$\beta_6 = m_1 \cdot L_2^2$
$\beta_7 = (m_1 \cdot L_2) + (m_2 \cdot r_2)$
$\beta_8 = m_2 \cdot L_3^2$
$\beta_9 = m_1 \cdot L_3^2$
$\beta_{10} = (m_3 \cdot r_3) + (m_2 \cdot L_3) + (m_1 \cdot L_3)$
$\beta_{11} = (m_2 \cdot L_3) + (m_1 \cdot L_3) + (m_3 \cdot r_3)$
$\Omega_1 = m_1 \cdot r_1^2$
$\Omega_2 = m_2 \cdot r_2^2$
$\Omega_3 = m_3 \cdot r_3^2$
$\beta_{12} = m_2 \cdot r_2$
$\beta_{13} = m_2 \cdot r_2 \cdot L_3$
$\beta_{14} = m_3 \cdot r_3$
$\beta_{15} = m_2 \cdot L_3$
$\beta_{16} = m_2 \cdot r_2 \cdot L_3$

Abbreviations:
NT = net torque
TAA = torque due to thigh angular acceleration
TAV = torque due to thigh angular velocity
LAA = torque due to leg angular acceleration
LAV = torque due to leg angular velocity
FAA = torque due to foot angular acceleration
FAV = torque due to foot angular velocity
HLAX = torque due to hip linear acceleration in the *x*-direction
HLAY = torque due to hip linear acceleration in the *y*-direction
GRAV = torque due to gravity
MT = muscle torque
IA = interaction torque

Ankle Torques

$NT_1 = (I_1 + \Omega_1) \cdot \ddot{\theta}_1$

$TAA_1 = -\beta_1 \cdot \cos(\theta_1 - \theta_3) \cdot \ddot{\theta}_3$

$TAV_1 = -\beta_1 \cdot \sin(\theta_1 - \theta_3) \cdot \dot{\theta}_3^2$

$LAA_1 = -\beta_2 \cdot \cos(\theta_1 - \theta_2) \cdot \ddot{\theta}_2$

$LAV_1 = -\beta_2 \cdot \sin(\theta_1 - \theta_2) \cdot \dot{\theta}_2^2$

$HLAX_1 = -\beta_3 \cdot \sin\theta_1 \cdot \ddot{x}_3$

$HLAY_1 = \beta_3 \cdot \cos\theta_1 \cdot \ddot{y}_3$

$GRAV_1 = \beta_3 \cdot \cos\theta_1 \cdot 9.8$

$MT_1 = NT_1 - HLAX_1 - HLAY_1 - TAV_1 - TAA_1 - LAV_1 - LAA_1 - GRAV_1$

$IA_1 = TAA_1 + TAV_1 + LAA_1 + LAV_1 + HLAX_1 + HLAY_1$

Knee Torques

$NT_2 = (I_2 + \Omega_2) \cdot \ddot{\theta}_2$

$TAA_2 = -(\beta_4 \cdot \cos(\theta_2 - \theta_3) + \beta_5 \cdot \cos(\theta_2 - \theta_3) + \beta_1 \cdot \cos(\theta_1 - \theta_3)) \cdot \ddot{\theta}_3$

$TAV_2 = -(\beta_4 \cdot \sin(\theta_2 - \theta_3) + \beta_5 \cdot \sin(\theta_2 - \theta_3) + \beta_1 \cdot \sin(\theta_1 - \theta_3)) \cdot \dot{\theta}_3^2$

$LAA_2 = -(\beta_6 + \beta_2 \cdot \cos(\theta_1 - \theta_2)) \cdot \ddot{\theta}_2$

$LAV_2 = -(\beta_2 \cdot \sin(\theta_1 - \theta_2)) \cdot \dot{\theta}_2^2$

$FAA_2 = -(\beta_2 \cdot \cos(\theta_2 - \theta_1) + (I_1 + \Omega_1)) \cdot \ddot{\theta}_1$

$FAV_2 = -(\beta_2 \cdot \sin(\theta_2 - \theta_1)) \cdot \dot{\theta}_1^2$

$HLAX_2 = -(\beta_3 \cdot \sin\theta_1 + \beta_7 \cdot \sin\theta_2) \cdot \ddot{x}_3$

$HLAY_2 = (\beta_7 \cdot \cos\theta_2 + \beta_3 \cdot \cos\theta_1) \cdot \ddot{y}_3$

$GRAV_2 = (\beta_7 \cdot \cos\theta_2 + \beta_3 \cdot \cos\theta_1) \cdot 9.8$

$MT_2 = NT_2 - HLAX_2 - HLAY_2 - TAV_2 - TAA_2 - LAV_2 - LAA_2 - FAV_2 - FAA_2 - GRAV_2$

$IA_2 = TAA_2 + TAV_2 + LAA_2 + LAV_2 + FAA_2 + FAV_2 + HLAX_2 + HLAY_2$

Hip Torques

$NT_3 = (I_3 + \Omega_3) \cdot \ddot{\theta}_3$

$TAA_3 = -(\beta_1 \cdot \cos(\theta_1 - \theta_3) + (\beta_4 + \beta_5) \cdot \cos(\theta_2 - \theta_3) + \beta_8 + \beta_9) \cdot \ddot{\theta}_3$

$TAV_3 = -((\beta_4 + \beta_5) \cdot \sin(\theta_2 - \theta_3) + \beta_1 \cdot \sin(\theta_1 - \theta_3)) \cdot \dot{\theta}_3^2$

$LAA_3 = -((\beta_4 + \beta_5) \cdot \cos(\theta_3 - \theta_2) + \beta_6 + \beta_2 \cdot \cos(\theta_1 - \theta_2) + I_2 + \Omega_2) \cdot \ddot{\theta}_2$

$LAV_3 = -(\beta_2 \cdot \sin(\theta_1 - \theta_2) + (\beta_4 + \beta_5) \cdot \sin(\theta_3 - \theta_2)) \cdot \dot{\theta}_2^2$

$FAA_3 = -(\beta_1 \cdot \cos(\theta_3 - \theta_1) + \beta_2 \cdot \cos(\theta_2 - \theta_1) + I_1 + \Omega_1) \cdot \ddot{\theta}_1$

$FAV_3 = -(\beta_1 \cdot \sin(\theta_3 - \theta_1) + \beta_2 \cdot \sin(\theta_2 - \theta_1)) \cdot \dot{\theta}_1^2$

$HLAX_3 = -(\beta_{10} \cdot \sin\theta_3 + \beta_7 \cdot \sin\theta_2 + \beta_3 \cdot \sin\theta_1) \cdot \ddot{x}_3$

$HLAY_3 = (\beta_{10} \cdot \cos\theta_3 + \beta_7 \cdot \cos\theta_2 + \beta_3 \cdot \cos\theta_1) \cdot \ddot{y}_3$

$GRAV_3 = (\beta_{11} \cdot \cos\theta_3 + \beta_7 \cdot \cos\theta_2 + \beta_3 \cdot \cos\theta_1) \cdot 9.8$

$MT_3 = NT_3 - HLAX_3 - HLAY_3 - TAA_3 - TAV_3 - LAA_3 - LAV_3 - FAA_3 - FAV_3 - GRAV_3$

$IA_3 = TAA_3 + TAV_3 + LAA_3 + LAV_3 + FAA_3 + FAV_3 + HLAX_3 + HLAY_3$

References

Hoy MG, Zernicke RF. Modulation of limb dynamics in the swing phase of locomotion. *Journal of Biomechanics* 18: 49-60, 1985.

Schneider K, Zernicke RF, Ulrich BD, Jensen JL, Thelen E. Understanding movement control in infants through the analysis of limb intersegmental dynamics. *Journal of Motor Behavior* 22: 493-520, 1990.

Winter DA. *The biomechanics and motor control of human gait: normal, elderly and pathological.* Waterloo, ON: University of Waterloo Press, 1991.